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RECOLLECTIONS AND LETTERS OF SIR JAMES MACKENZIE*

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BOSTON

THE career of James Mackenzie is without a parallel in medical annals, and the facts of his life read like a romance. A poor boy, the son of a Scottish farmer, he left school at the age of fifteen. For him schoolbooks had no attraction, but the colored lights in the windows of a chemist's shop lured him, and he became an apothecary's apprentice. That this was not the best foundation for medical studies everyone must agree. Finally he realized his mistake, and at the relatively advanced age of twenty-one he began his medical studies in the University of Edinburgh. He graduated in 1878, and after serving a year's residence in the Royal Infirmary became an assistant in a medical "firm" in the manufacturing city of Burnley, England. This firm had been established about eighty years earlier, and the successors of the founders carried on a large general practice. There was nothing in his environment to stimulate him to do anything more than conscientious routine work in the diagnosis and treatment of cases representing the entire range of medical practice, yet he developed new methods of clinical investigation and made important discoveries in diseases of the heart and in the nature and significance of pain in visceral disease. He showed that the sphygmograph, which had come to be regarded as a physiological toy, could be made to yield information of great clinical value.

After twenty-eight years of general practice, he broke all precedents by moving from a provincial English town to London; he became a consulting physician, limiting his practice to diseases of the heart. He had no school or hospital connections, and was practically a stranger in the metropolis; his name was almost unknown to London physicians. Every avenue leading to advancement seemed closed to him. He had a wife and two children to support, and at first there were no patients. His biographer says that his income during that first year in London was only £114. Then, some time during his second year, he awoke to find himself famous. His book on the heart had a great sale, and his name became a household word. Patients in large numbers were referred to him by physicians in this country and Canada as well as in Great Britain. A new department for cardiac disease was established for him at the great London Hospital. He was made a fellow of the College of Physicians and a fellow of the Royal Society, and the honor of knighthood was conferred upon him by the King. At the high tide of prosperity he gave up everything he had obtained in London and moved to the small town of St. Andrews in Scotland, to establish an institute for clinical research, largely at his own expense. Increased honors reached him there, and he was made Physician-to-the-King in Scotland. In August, 1924, because of ill health he retired to London, where he passed the last months of his life. His death on January 25, 1925, was due to disease of the heart, the organ with which his name will always be associated. His mental activity and energy continued to the last, and he wrote the final sentences of a book summarizing five years' work at St. Andrews less than forty-eight hours before he succumbed to coronary thrombosis.

Sir James Mackenzie made three visits to America; the first, a nonmedical trip, in 1880 after recovery from typhoid fever, when he traveled as far west as Yellowstone National Park. Since he had no money, being only two years out of medical school, he probably accompanied a patient. The second trip was in 1906, when he attended the meeting of the British Medical Association in Toronto. He was then a general practitioner, and he came and went largely unnoticed by the recognized leaders of the profession. During his third visit in 1918 he was everywhere received as a distinguished representative of British medicine. He was selected at that time by the British government as a member of a small commission of medical men to visit the United States, and he attended

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among other meetings those of the Massachusetts Medical Society and of the American Medical Association. He was always a general practitioner at heart. When in Boston in 1918, as he was leaving my home in Brookline, we met my friend and neighbor, Dr. George K. Sabine, a leading family doctor in that town. Sir James grasped his hand warmly and said it was indeed a pleasure, after associating only with surgeons and consulting physicians, to meet one of his own kind, a general practitioner.

My first acquaintance with Dr. Mackenzie was made at the Toronto meeting in 1906, which I attended with my friend, Dr. Henry A. Christian. Although representatives of British medicine whose reputations were world wide were at the meeting, the one who impressed us most was the general practitioner from Burnley, James Mackenzie. He was then fifty-three years of age. We saw a tall, well-built man with a fine head, noble brow and kindly eyes, who spoke with a contagious enthusiasm. Two symposiums were held by the medical section; one dealt with blood pressure, the other with heart block. Mackenzie read a paper in each of these. This was certainly an unusual distinction. On the same program were such names as Ludwig Aschoff, Sir Clifford Allbutt, Sir William Broadbent, and George A. Gibson, of Edinburgh. Mackenzie's paper was the third in a series on heart block that he had written within a short period. It represented the results of long and faithful investigation by means of simultaneous records of the jugular and radial pulses. He reported a most unusual case of transient heart block that occurred when the patient swallowed, and proved its existence by clear, convincing tracings. After his death the writer of a memorial sketch[1] in the *Lancet* stated that it was this paper that first made his labors clear "to anything like a large audience." When I was in London two years later a leading physician referred to Mackenzie in a condescending manner as "Heart-block Mackenzie." At the Toronto meeting, Mackenzie also demonstrated his ink-writing polygraph, newly invented, which enabled him to make continuous pulse tracings of the radial and venous pulse for many minutes. The jugular pulse tracings made with other types of apparatus, which two physicians presented, did not compare with those shown by Mackenzie. In fact they were so poor that definite interpretation of the tracings was difficult if not impossible.

After the Toronto meeting Mackenzie came to Boston, accompanied by his friend, Dr. Arnold Lea. He wished particularly to meet Professor William T. Porter of the Physiological Department at the Harvard Medical School, with whose important paper on the filling of the heart he was familiar. It was characteristic of him then, as it had been in earlier years, to seek help from physiologists. Dr. Porter had organized and developed a company which made physiological apparatus for the use of students in medical schools. Unforeseen obstacles prevented the fulfillment of Dr. Mackenzie's hope that his ink-writing polygraph might be manufactured by Dr. Porter's instrument makers. During this visit Mackenzie gave a demonstration of his instrument one evening after dinner to a group of young men that I assembled.

He was particularly interested in a case of mitral stenosis, with absolutely irregular pulse, at my outpatient clinic at the Massachusetts General Hospital, and he referred to it in a letter written a year later. He pointed out to those gathered about him that the typical presystolic murmur of mitral stenosis was absent, and that it is never found after the auricular wave has disappeared from the venous pulse.

In 1902 he published his first book, *The Study of the Pulse,* which had only a small sale in England and in this country. This book, considered by some his greatest and most original work, contained reproductions of over three hundred carefully analyzed tracings that he had made in cases observed in his private practice. These consisted of records of the arterial, venous and hepatic pulses and many cardiograms. Nothing to compare with this collection had ever been published. He began to make tracings of the jugular pulse in 1891. For years he used for this purpose a Marey tambour attached to a Dudgeon sphygmograph, a simple equipment that could be carried in the pocket. His first paper — and an excellent one — dealing with the venous pulse was published in 1892 in Volume I of the *Journal of Bacteriology and Pathology.* He showed clearly that Friedreich's interpretation of the waves in the venous pulse, universally accepted as correct for thirty years, was wrong, in that the wave caused by the contraction of the auricle was attributed to the ventricle. Mackenzie proved that this error was due to incorrect timing of events in the cardiac cycle. In the preface to his book, *The Study of the Pulse,* he writes:

> This volume has been written amid the distractions of the life of a busy general practitioner. I have seldom been able to give an uninterrupted hour's study to the subject. While working out some argument, interruptions have often been fatal to its completion, as it has been days and even weeks before I have again been able to resume it. While the working out of these problems has been a source of interest and of

pleasure, the labour of writing them out has been a weariness to the flesh. This I do not offer as an excuse, but as an explanation.

The book had been recommended to me by Dr. Walter I. Steiner, of Hartford, Connecticut, who was possibly the first American to recognize its value, but I had not read it. I told Dr. Mackenzie during his Boston visit that I was going to buy his book. He replied: "Don't. Nobody does. I have a shed full at home and will send you a copy." Instead of mailing the book, he waited until he could send it by a messenger. Some months later Dr. George W. Ross, of Toronto, arriving in Boston from England, brought me the book. Ross had spent a short time in Burnley with Mackenzie, observing his work, and was probably the first physician from this side of the Atlantic to visit Burnley for the purpose of learning Mackenzie's methods. There he could get a knowledge of certain aspects of cardiac disease not attainable elsewhere in the world. What Mackenzie had to offer can be appreciated from the following letter written in Burnley, and dated May 20, 1907:

> I am very glad things are prospering with you, though I am sorry you could not come and see Burnley. My reason for regret is that I have here such a wonderful selection of cases illustrating a great many forms of heart change, unsuspected and unrecognized, and I fear much that my removal will take me out of touch of these cases. Still I shall be glad to renew our acquaintance when you come to London next year.
>
> I have just returned from attending the meetings of a newly formed Association of Physicians in London. I expounded some new views as to the meaning of the continual irregular heart and the direct causes of heart failure in these cases, which views were received appreciatingly, but as my audience did not appreciate my facts, I fear they were not convinced. I saw Osler there and also your admiring friend Martin of Montreal, who hopes to spend next Thursday night here before sailing from Liverpool. I have also had a pleasant visit from Dr. Grosh of Toledo, who is to be expounding some views on the venous pulse at the meeting on June 6th at Atlantic City.
>
> My book that Ross left you is sadly behind the times, but it gives an idea how to set about this sort of work. Your hands are too full with your own line of study and as this requires a long and painful training, you might start some of your promising juniors — it will amply repay them for the trouble. I find Ross a most apt pupil, and with him in Canada and Grosh in Toledo, I am hoping that these two sources will leaven a big lump of your vast continent. They are also promising good things at Johns Hopkins.
>
> Remember me to Joslin, Christian, and the other bright spirits who made my visit to Boston so delightful. Arnold Lea occasionally visits me, and we recount our Boston experiences with great gusto — particularly the charming Williams' most interesting yarns.

Osler appears to have been the first physician of distinction in England to appreciate Mackenzie's worth, and we learn from Cushing's *Life of Sir William Osler* that very shortly after he settled in England, in July, 1905, he made a visit to Burnley. Of this, Mackenzie wrote Cushing: "One of Osler's great charms was the kindly interest he took in obscure workers in any field of medicine; and in 1905 when I was a general practitioner in a remote town in Lancashire he paid me a visit; and though my work was not that in which he was directly interested yet his appreciation was in itself a very great encouragement." Mackenzie told me that he had demonstrated to Osler at that time a case of mitral stenosis in which the typical presystolic crescendo murmur had disappeared as a result of paralysis of the auricle, — indicated by an absence of an *a* wave in the venous tracing, — but that he could not convince Osler of the correctness of his observation.

Possibly about the same time, but probably a year or two earlier, Mackenzie received a visit from the great Dutch physician, Wenckebach, whose contributions to a knowledge of the arrhythmias rank with his own. In Wenckebach's[2] monograph on this subject published in 1903 he gives Mackenzie great praise. The latter in turn thought so highly of Wenckebach's work that he induced a Burnley ophthalmologist, Dr. Snowball, to translate the German text into English, and secured its publication. This book, well printed and attractively bound, probably had a very small sale, because the general medical world at that time knew too little of the subject to appreciate its importance.

Osler was also the first to bestow praise on Mackenzie at a large medical gathering. At the Congress of American Physicians and Surgeons, held in Washington in May, 1907, in the course of an address on "The Evolution of the Idea of Experiment in Medicine" he said, "In every country there will be found strong men like Weir Mitchell, Mackenzie of Burnley, and Meltzer and Christian Herter who find it possible to combine experimental work with practice."

Mackenzie probably made the bold decision to settle in London in the hope that he could find able young men who would use the new methods he had devised, and he doubtless thought that if he were located in a large medical center he would have greater opportunities for carrying on investigations with the aid of such outstanding men of science as Cushny, the pharmacologist, and Arthur Keith, the anatomist. He would also be in a better position to acquaint the medical profession with the new knowledge of heart disease that he had brought to light.

Mackenzie was a true missionary of science, with a zeal that could not be quenched by opposition,

or what is more difficult to bear, indifference. In Manchester, the nearest medical center to Burnley and the seat of a medical school (Owen College), he tried in vain to get his methods adopted. He once told me that for fifteen years he attempted to interest the physicians in Manchester by giving papers and demonstrations. There would be no discussion. After the meeting he would find himself alone in the room. He would pack up his polygraph and tracings and retrace his steps to Burnley, forty miles distant.

The next letter I have preserved was written on November 5, 1907, shortly before he left Burnley to work in the larger field of London.

> I was glad to hear from you again, and pleased with the idea that you intend taking up heart work. I am afraid, and yet for you, rather glad, that you won't do this, for the reason it involves a lot of drudgery and wearisome work that will take up far more time than you can spare. You are now getting so busy and interested in other matters that you will not find the time. And yet it is a wonderful field it has opened up. These recent methods are generally assumed to be of interest in an academic sort of way but of no practical utility and recent writers of books refer to them in such a manner that this impression is encouraged placing the new methods in a sort of appendix. Now I find nothing so helpful in diagnosis, prognosis, and treatment as the application of the principles derived from them. I am just now in the throes of a book, where I attempt to bring them in the every day practical examination of patients. The undertaking involves [such a] breaking away from the well established methods of book making that I sometimes despair of doing justice to the subject. When you come to London I hope to be able to demonstrate the essentially practical nature of these new methods. I wish, however, it had been Burnley you were coming to, for I have here such a selection of cases that astonish all who visit me.
>
> My reason for writing you so soon is that I want to know if you have kept the heart of that lad with mitral stenosis. I have now I think been able to establish that in mitral stenosis the rhythm of the heart starts at a node of tissues at the beginning of the a-v bundle. Some of the evidence is in a reprint I post with this. In certain rare cases there is a tendency for this rhythm to start for brief periods giving rise to attacks of paroxysmal tachycardia though the rate may not be greatly increased. I have had several of these cases and a very typical one died in an attack, but I mislaid the heart after noting the mitral stenosis. I feel fairly certain that if your patient's heart be microscopically examined there will be found an extension of the sclerotic process affecting the a-v bundle. Do you think you could get it examined?
>
> It is curious your letter came when I was constructing a chapter on heart affections in neurotic people and had just finished the chapter on heart block which I take to be the cause in your man with the slow pulse. I have to go some forty miles tomorrow to see a very similar case. The cause I suspect is an extension of the sclerotic process cutting the bundle in two. When you come to London I will take you to Keith — one of the Lord's anointed — and he shall show you all these things.
>
> I have had two most excellent articles from Hewlett, and I shall write him for a reprint of the articles you mention.
>
> I had a wealthy lady with rheumatoid arthritis in her arm and she wanted another opinion so we motored down to Oxford and saw Osler. He was as chirpy as ever and told me you were going with him and Gibson to Vienna and he asked me to join the party. I fear it is one of those good things that will be denied to me.
>
> We go to London on December first so if you are so good as to write to me, address me at 17 Bentinck St. W., London.
>
> My wife bids me say she expects you to put up at that address, i.e., if you will be content with homely fare after the sybarite enjoyments of Oxford. I shall introduce you to these rare spirits — Cushny, Keith, Starling, Bayless, etc. You would do better work in London than with Krehl.

The book he was then writing, *Diseases of the Heart,* was published in the fall of 1908 and proved extraordinarily successful. He attributed to it the rapid growth of his practice in London after the first barren year. It was translated into German, French and Italian.

This letter reveals that at that time he was absorbed with the problem of the cause of the absolutely irregular pulse now known to be due to auricular fibrillation, and that he thought he had evidence that in this type of irregularity in mitral stenosis the rhythm begins in the auriculoventricular node; he therefore termed this rhythm "nodal rhythm." Although he then mistook its true nature, he recognized and differentiated this important group of the arrhythmias at a time when leading clinicians in Europe and America were ignorant of its existence. For years the pulse in those cases was described as intermittent and irregular, and no attempt was made to distinguish this arrhythmia from the irregularity of the pulse due to frequent extrasystoles. Mackenzie, on the other hand, stated in a paper published in 1908 that he had studied no less than six hundred cases of what is now called auricular fibrillation.

As early as 1898 he observed in a case of mitral stenosis that he had followed for six years that the auricular wave in the liver pulse, present in all previous tracings, disappeared, as did a "long murmur running up to and ending abruptly in the first sound, heard only at the apex." At the same time the pulse became irregular. He concluded that the patient had developed auricular paralysis. At the autopsy the auricles were greatly distended into thin-walled sacs "with a few strands of muscular fibres scattered over them." This explanation of the disappearance of the *a* wave in the venous pulse as due to paralysis was nearly correct, for the auricle, the seat of fibrillation, does not contract. The relation is certainly

l. 224
941

close between the motion of a muscle that consists of a fine quiver and an actual paralysis. It is clear that Mackenzie's theory of nodal rhythm advanced in 1907 was much farther from the truth. He held to this theory until late in 1909, when Thomas Lewis showed that auricular fibrillation was the cause of the persistent irregularity. It was Mackenzie who stimulated Lewis to investigate the subject with the newly invented electrocardiograph. In the fourth edition of his textbook Mackenzie returned to his original designation, namely, paralysis of the auricle.

The next letter, dated January 31, 1908, was the first I received after he had moved to London. The book was nearly completed, and he was already in close touch with Cushny, who was investigating a subject of great interest to Mackenzie, namely, ventricular rhythm. This was the term applied to the contractions originating in the ventricles in cases of heart block.

> Your letter relieved me. I had been told you were coming over in March and as I will have to go to Scotland until the end of March I am so afraid I might miss you. I am certain to be here all April, and will be free from the writing of my book which has engrossed all my energies for the last ten months and particularly so the two months I have been in London. I look forward to seeing you and will hope to make your visit here interesting and profitable. I regret, however, that I don't have any patients to show you, as there is absolutely no likelihood for my getting such a hospital appointment as I would care to accept, but I have one or two disciples and we may get the use of their cases.
>
> I am glad your article for Osler is finished and I shall look forward to its perusal. I was interested in the fact that you had suggested His's bundle as the seat of irregularity. I remember a lecture of Clifford Allbutt in 1902, I think it was, in which he suggested "Gaskell's bridge" as the starting place. What a pity it was that you did not seek to carry out the suggestion by seeking for proof. The more searchers we get the nearer we will get to the truth. Though I got the idea about 1904, I am not quite convinced of its truth, for it has not been proven, and in my papers I make the suggestion boldly in order to stimulate others; and if they prove me wrong then I will rejoice at the discovery of the truth. In my book I do not take a strong standpoint, only suggest. I may say Professor Cushny has been able to produce the "ventricular rhythm" in dogs by aconitine and we are trying to get to its origin experimentally — but the difficulties are very great.
>
> If you are really interested I think I will be able to start you well on your way during your stay with us. I am certain you will be pleased with the definite results you can get, especially when you have been engaged in the extremely difficult problem of metabolism.
>
> I am glad you liked Starling. He is a delightful man as well as a great physiologist. You are right in regard to our physiologists. They are splendid men and so simple. Gaskell, for instance, is far ahead of any physiologist; even Engelmann, who has such a reputation, has only followed Gaskell's lead. It is the man who originates that is the great man, not the man who does the spade labor. Gaskell's work on the heart will place him next to Harvey in my opinion, and his work in the nervous system will give him a very high place in science.
>
> I have been reading a lot of heart work lately, and I like the English better than the French and German. You will find that clinically and for practical recognition of conditions that writers like Broadbent are far ahead of any others. I have been reading Krehl, Romberg, and Hoffman and I am greatly disappointed in their clinical work. They are besides extremely badly informed of what other writers are doing and though they quote a lot of names you will find on deeper inquiry that the names are of little value and the reasons for their quotation . . . [illegible writing]. I don't want to flatter you but the papers you sent me were far more suggestive than any of these authors. They take such narrow views and expressed their views as if they were the only possible ones, and no more to be said. This "finality" particularly by French and German writers is one of the most amusing things I came across. I hope when you come here you will realize the strength of English clinicians.

In a paper published in 1904 I[3] had said that a fatty change "in His' bridges, which transmits the contraction from auricle to ventricle, might impair the action of the heart while an equal fatty alteration elsewhere would not. Unfortunately no exact data are available. . . ." Mackenzie was right in criticizing me for not acting on the suggestion I put forward. I did not know at the time that, five years before my paper appeared, Wenckebach and His had independently suggested a lesion of the auriculoventricular bundle as the cause of heart block.

From July, 1906, onward I had under my care a Mr. Baker, who, because he lived near Boston, was referred to me for treatment with artificial "Nauheim baths," by my friend Dr. John H. Musser, whom he had consulted in Philadelphia. These were carbon dioxide baths of various strengths given at definite temperatures. Dr. Musser believed that the patient had beginning myocardial disease, and at that time it was generally held that carbon dioxide baths would strengthen the heart muscle. On September 1, 1907, Mr. Baker noticed slight difficulty in breathing, and his pulse rate, which had been normal, suddenly became slow. It was 38 to the minute when I examined him two days later, and subsequently I counted it as low as 28. After the bradycardia had continued for four months, the rate returned to normal. Because the patient was going to England in the spring of 1908, Dr. Musser agreed with me that it would be a good idea to have Dr. Mackenzie examine him. We thought he had had heart block, but definite proof was lacking. Mr. Baker was then fifty-three years old, the pulse rate

was normal and he was free from symptoms. I mention his name because Dr. Mackenzie referred to him repeatedly in his letters. He evidently never lost interest in his patients or forgot them. In the spring of 1924, sixteen years after he had examined Mr. Baker and less than a year before his own death, he wrote a note expressly "to hear how Mr. Baker had gone on."

I was present in Mackenzie's consulting room at 17 Bentinck Street when he examined Mr. Baker. Not much time was spent on the history or physical examination, and only a very few notes were made. The patient's pulse was regular and about 79 to the minute. Soon the ink-writing polygraph was brought out, and a continuous tracing of the radial and jugular pulse was made. Yards and yards of the paper ribbon passed through the machine and accumulated in wide loops on the floor. Mackenzie wanted to get the information he thought might be furnished by an extrasystole, but the pulse continued perfectly regular for many minutes. Finally after about twenty minutes, one extrasystole appeared on the tracing. Although the pulse was traced for some time longer, no other extrasystole was obtained. Figure 1 shows the polygraph tracing recorded at that time, April 1, 1908. The analysis made by Mackenzie was contained in a letter I received from him after I reached Heidelberg:

> I promised to send you the tracing of Mr. Baker's auricular extra-systole.
>
> The features brought out in the tracing are, a larger venous pulse than usual, and associated with it an increase in the heart's dullness, indicating a certain degree of dilatation. The tracing shows an increase in the *a-c* interval, slight but distinct. Normally at this rate of the heart's action the *a-c* interval rarely exceeds one fifth of a second, here the intervals (spaces A) are distinctly more than one fifth. The extra-systole is of auricular origin (*a'* in the jugular tracing). It is followed by a carotid wave, *c'*, which I recognize as carotid because it is the same distance apart from the preceding wave, *c*, as the radial extra-systole, *r'*, is apart from the preceding radial beat, *r*.
>
> The *a'-c'* interval (space A') is greatly increased. This increase is rare in auricular extra-systole and is a further evidence of the impairment of the conduction of the a-v bundle. These undisputed evidences of delayed conductivity lead me to agree with your diagnosis of the condition when the pulse was slow — namely, that Mr. Baker had a transient heart block. On this point I will be able to speak with more certainty when I see the tracings. My diagnosis, — cardio-sclerosis, affecting the muscle wall, and extending to and partially destroying the a-v bundle.

The tracings, the arrival of which he was awaiting, had been made by Dr. George W. Norris, then Dr. Musser's assistant, at a time when Mr. Baker had bradycardia. On April 14 he wrote that the tracings had been received, and that they

> confirm my diagnosis and render Mr. Baker's case one of great scientific interest, as few cases have such a good history of the change and confirms me in the view I have expressed in my book of the relationship of extra-systoles and "nodal rhythm" to heart block.
>
> The prognosis is by no means bad, if he will be content with a crippled existence. If you should have to write Dr. Norris, tell him I think highly of the manner he has analyzed the tracings. There are not six men in the United Kingdom that could have done it.
>
> P. S. I have kept the original intact and copied in accurately the auricular extra-systole. If the American tracings are not of use to you I would like them, but you should keep them and publish a full account of this case in which case I shall let you have the original tracing we took together.

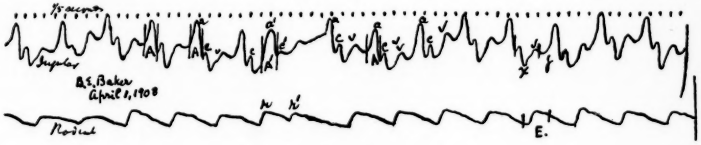

FIGURE 1.
Tracing made by Dr. Mackenzie of a case of partial heart block.

During the following years Mr. Baker continued to have recurrent attacks of complete heart block. Pulse tracings that I took during one attack were sent to Mackenzie with those of other cases of abnormal rhythm. On April 4, 1909, he wrote:

> Your interpretation of the tracings is correct in each case. Note the difference in the *a-c* interval when there is heart block and when there is not (space A). I am sorry to hear of his recurrent attack. I shall look forward to the results of your endeavor to treat them. I expect a quiet God-fearing life will be best. . . . I got your letter yesterday and on the same evening I had an identical tracing of heart block sent me for my opinion from Sheffield. . . . If you can spare a bit of Baker's tracings I shall be glad to have it.

The statement that he looked forward to my endeavor to treat the attacks has a hidden meaning, which shows his tolerance to his friends who

held views regarding treatment with which he strongly disagreed. He knew that I believed that carbon dioxide baths strengthened the heart, and that I was employing them in the treatment of Mr. Baker. When Mackenzie was in Boston in 1906 I showed him the record of a patient with congestive heart failure who recovered after a course of such baths. He was quite right in failing to consider this favorable result as valuable evidence. I remember to this day his reply: "Patients usually recover from their first attack of heart failure, no matter what treatment is employed." I pointed out to him that Krehl and Romberg, who were regarded as great authorities in heart disease, advocated treatment by carbon dioxide baths in their writings. He told me that I quoted Krehl and Romberg too much. I should make my own observations, do my own thinking and draw my own conclusions. I had worked under Krehl and doubtless was influenced by his teachings more than I should have been.

In his textbook, *Diseases of the Heart,* Mackenzie inserted a strong condemnation of the Nauheim baths. At that time they had a high reputation in England. He told me at the time he was writing his book that a professional friend who had read it in manuscript urged him to omit the criticism. This he refused to do. He had visited Nauheim, and did not condemn the method without reason. In the printed text he said, "Though I enter into this matter reluctantly, I conceive it nonetheless a duty to give my views on it, particularly as I am impressed with the injury done to individual patients through the unmerited reputation of the Nauheim baths among the medical profession." Mackenzie was right. The blast he directed against the Nauheim baths, natural and artificial, was effective, and nothing in their favor has supplanted the evidence he assembled against them over thirty years ago. Their use, in this country at least, lessened rapidly, and this was due in no small part, I believe, to Mackenzie's vigorous condemnation.

Before dismissing the case of Mr. Baker, an incident may be related that throws light on Mackenzie's attitude toward the financial side of medical practice. He was free from mercenary motives in moving to London. The character of many an able physician has been marred by an "itching palm." Not so Mackenzie. Mr. Baker was a wealthy manufacturer. He was, I think, the first patient referred to him from America, and he came on the recommendation of one of the leading physicians in the United States, Dr. John H. Musser. One day on the steamer going to England, Mr. Baker asked me how much Dr. Mackenzie would probably charge him. I told him I did not know, but since Mackenzie was an international authority I thought he might rightly charge him any amount between $75 and $150. Mr. Baker seemed relieved and said that would be satisfactory. He added, "I feared he might stick me $500." As I have already said, his total income the first year in London was only £114; hence, his receipts must have been very small up to the time I brought Mr. Baker to him. One morning after breakfast, I think on the day of the consultation, I asked Dr. Mackenzie how much he was going to charge my patient. "Three guineas is my fee." "If you do not charge Mr. Baker more than that," I replied, "it will make an unfavorable impression upon him. He will doubt whether I have brought him to a great heart specialist. He expects to pay you much more than that, and your opinion in his case is worth much more." It took much persuasion to induce Dr. Mackenzie to raise his fee. I think he charged Mr. Baker $50 or $60; I know it was less than the minimum figure I had mentioned. I did not know at the time how much he needed money. Lady Mackenzie told Mackenzie's biographer, Dr. R. MacNair Wilson,[4] years later, "We were really and truly poor people." Their hospitality was unbounded. On two visits to London in 1908 I was their house guest all the time I was in the city. In the many talks I had with Mackenzie on those occasions he never expressed any fear that his London venture might end disastrously because of his failure to build up a practice. In fact, he never talked about financial matters.

After he had been in London a couple of months, Mackenzie had written me that there was "absolutely no likelihood for my getting such a hospital appointment as I would care to accept." But on May 24 he wrote: "I have the offer, which I will probably accept, of having charge of wards in a hospital during August and September, beginning about August 7th. . . . I wonder if you could delay your return to London until after August 7th, and come and work a short time with me in the wards. Turn this over in your mind and let me know." And on June 8 he wrote, "So far as I can see at present I shall get the wards about August 7th and if so we can have two or three days' discussion on the points that have arisen in your work in Heidelberg." He did not get the control of any wards, and this must have been a keen disappointment, but he never offered any explanation to me. He had learned, in Osler's words, "to consume his own smoke." I think he must have referred to the wards at the London Hospital under the care of

Henry Head, who was on a vacation at the time. We did visit the hospital one day, traveling to the east end of London on a bus. Mackenzie went to the basement of his home and smoked some tracing paper just before we started. He introduced himself to the sister in charge of the ward and said that Dr. Head had given him the privilege of examining the patients on the wards. We had a cool reception. I suspect Dr. Head had neglected to speak to the nurse. She simply bowed, and we began to walk from bed to bed until, without assistance, we found patients with heart disease. Mackenzie took out his polygraph and began to make tracings of the pulses of patients who had irregular rhythm. There was a house officer on the opposite side of the ward, but he did not offer to help us. In fact, he seemed to regard us with some suspicion. Finally the sight of the moving levers recording the radial and venous pulse aroused his curiosity. He crossed the ward and asked Mackenzie if that was a Hill–Barnard blood-pressure apparatus. "No," was the reply. "It is called a polygraph and was invented by a man named Mackenzie." Evidently disappointed, the young doctor walked away without another word. The polygraph and its inventor meant nothing to him. Only a few years later a new department for cardiac disease was created for Mackenzie in this same hospital. His nomination was made by no less a person than Lord Dawson of Penn, the King's physician.

In his earliest paper on the venous pulse, published in 1892, Mackenzie believed that the ventricular type, as he termed it, indicated dilatation of the right ventricle and tricuspid regurgitation. He held this view for years, in fact until he found that it was always associated with what he called "nodal rhythm," auricular fibrillation. In April, 1909, he wrote:

> The variation in the jugular pulse in undoubted tricuspid regurgitation puzzles me and I can only dimly and unsatisfactorily speculate as to the cause. If you can settle the matter it will be a good piece of work. You can have no one better qualified to help you than Professor Porter. I think I did wrong to follow Frey's description of the auricular pressure. I think now that Porter is the truer. Some day I hope to apply his results to the venous pulse. I have already got some helpful tracings that way. Remember me kindly to him.

The next letter dates from the St. Andrews period and was written in April, 1924, only four months before ill health compelled him to retire to London. In spite of physical disability his mind turned incessantly to advancing knowledge and combating error.

> I would strongly urge you to keep your instrument in good condition, because the polygraph is of far more use than the electrocardiograph. In the reprint upon cardiology which I sent you, you will see how much stress I am laying upon the output of the heart, and that it can only be registered by the sphygmograph, the electrocardiograph giving no information in regard to this important point. When you come to think of it, it is the capacity of the heart to supply the tissues with blood which we want to know, and that can only be done by ascertaining how the circulation is maintained in the body, and for this information we are dependent upon the patient's response to effort—the state of the pulse, and the presence or absence of signs of dropsy, etc. These essential matters are utterly beyond any instrument limited to the heart beat.
>
> I am carrying the matter further than is represented in the reprint, for the small imperfect beats are those which give rise to heart failure, and it is by their suppression that digitalis proves so beneficial.
>
> I see the old notion of operating on mitral stenosis is being revived. I wish surgeons would think of what the effect is of cutting scar tissue anywhere. It is only a small number of patients in whom the stenosis is a serious matter. The danger lies in the damage to the muscle, and almost to a certainty the cut in the scar tissue will unite again.
>
> Another absurd piece of surgery has been carried out by the cutting of the sympathetic in angina pectoris. Of course, if a patient has gout in the big toe, the cutting of the afferent nerve will relieve the pain, but it will not cure the gout. If you think for a moment of the state of those hearts which are figured in my book on "angina" with the damaged coronary artery, and the great mass of damaged muscle, what on earth is the good of cutting the sympathetic? The pain may diminish, but its presence is actually beneficial, in that it provides a measure by which the patient can tell how much effort he should undertake. It is not the pain that is dangerous in angina pectoris. No person ever dies of pain. The pain only indicates the presence of some morbid state, and consequently, by relieving the pain you don't remove the morbid state. I have given the details of patients in my book to show that the pain or the angina itself is not necessarily a dangerous complaint, and if you read the history of some of these cases, you will see that people with angina can live as long as the average.

Partly as a result of Mackenzie's teaching, and partly as a result of personal observation and experience over a period of ten years, I was convinced that the best treatment for angina pectoris was prolonged bed rest. Knowing that Sir James, although afflicted with frequent attacks of angina, had been keeping at work, I wrote him of the excellent results I had obtained and urged him to seek the advice of his friend, Sir Clifford Allbutt, who was an ardent advocate of the bed-rest treatment and who had acquainted me with his success. He wrote that even in a "terrible case of angina pectoris, great relief if not cure" resulted from six months in bed. When Sir James Mackenzie received my letter he had only recently returned to

London and, as I learned later, was without medical care. It is always a hazardous matter to give unsought advice to a sick friend, especially if he happens to be the victim of a disease of which he is acknowledged to be the greatest living authority.

The following letter was written from London on September 10, 1924:

> It was very good of you to write to me, and I appreciate very much your interest and your kindly suggestions. Your principle of treatment appeals to me. I have endeavored to follow it.
>
> There is one danger, however, in a rule of thumb treatment in that it is apt to be used indiscriminately, and therefore to submit patients to treatment who do not need it, and fails to treat others who do not benefit by it but who are even made worse by it. . . . In angina pectoris there are present morbid changes in the heart such as a narrowing of the coronary artery. This restricts the power of response of the ventricle so that effort produces pain. For a long time before pain arises there may have been persistent exhaustion which rest in bed does much to restore, but there are many circumstances other than effort which give rise to the pain. In my own case my first attack of pain was in 1908, and it arose in consequence of digestive indiscretion. I never had another attack of pain until two years ago, and then it was due to being chilled on a railway journey. For all these years I have known that the liability to pain was there, and ten years ago I used to be warned by the sense of constriction on going up hills, but invariably slowed down or stopped, and the pain was never induced. During the war I led the most strenuous life that ever I had done, without pain. Until eighteen months ago I played golf regularly, but on walking to the links, about a mile, I would have to stop every five hundred yards, caused by the constriction. Nevertheless I would play a round of golf without the slightest inconvenience.
>
> The two great causes of pain in my case are exposure to cold, and mental excitement. When I avoid these I have no pain. I cannot walk now more than a few yards before I get the warning, but as I always stop I do not have severe pain from this cause.
>
> All this means that my coronary arteries are slowly but surely becoming occluded.
>
> I have written this in order that you may see the principles which we are trying to establish at St. Andrews particularly in regard to the response to effort in the circumstances that lead to such attacks as those of angina Don't you think it a curious thing that notwithstanding the enormous amount of investigation that has been carried on that we are still as far from understanding the structures and processes concerned in the production of pain as were the pundits of the dark ages? Worse than that we don't even know what steps to take to get this knowledge. That is one of the problems I have been labouring at for forty years, and there is scarcely a physician who will take the trouble to find out what tissues, when stimulated, are capable of giving pain. In palpating the abdomen physicians and surgeons continually meet patients who complain of pain when pressure is made. No one, practically, takes the trouble to find out the structures which are being pressed upon which give rise to pain. Yet all physicians and surgeons resent the suggestion that they do not know how to palpate intelligently the abdomen.
>
> I write you this because I know you like to face problems. My wife and daughter join me in sending very best regards to you and your wife.

His last letter, dated November 18, 1924, was written only nine weeks before his death:

> I was much interested in your letter and I am glad you propose attacking the problem of angina. Your suggestion of publishing the details of a series of cases is admirable. I have felt greatly the absence of such observations, for everyone who writes on the subject gives either particulars of a few cases which are quoted merely to support his own view or generalizations without proof. It was to provide a wide survey and to give the evidence for every statement that I cited so many cases.
>
> But from your letter I see a danger in using them statistically. I had notes of 2000 cases. Half of them were too imperfect for use. Of the other 1000 I had full notes, which enabled me to divide them into groups chiefly of three kinds, according to their gravity — or rather, their duration. There was a group where the complaint advanced slowly and the individual reached an advanced age. A second group where the disease progressed with greater rapidly and a third group where the progress was rapid and the patient died about middle life. The first group was by far the largest — 700 or 800. The others much smaller. In the cases recorded in my book I give types of the groups independent of the number in a group. The largest of the groups were more of a type so that a few cases only were required. Of the others because of their gravity and individual character relatively more illustrative cases were given.
>
> There was no clear dividing line between the groups. The grouping was done for convenience. Now if you take your series of cases and give their history and start comparing them with those I have given with which group will you select? It will be perfectly easy to select one of your cases which had, after an attack of angina pectoris, led an energetic life for ten and fifteen years and compare it with one of mine who died a few months after his attack and attribute the improvement of your case to your treatment, and the death in my case to the lack of your treatment. This is the fallacy of statistics. . . .
>
> I have many cases I put to bed and keep them there for weeks and months, but I discriminate. Look at the diseased hearts pictured in my book and ask yourself what conceivable treatment is likely to restore these hearts. Such conditions must have taken many years to develop. Discrimination can only come through recognizing the rate of the progress of the diseased condition and then can only be drawn by *estimating the response to effort* — i.e., by the amount of effort the patient can undertake without distress. Rate of pulse, blood pressure, etc., afford no help in the matter. . . .
>
> I get along quietly, taking as much exercise as I can without distress. I have only laid up one day; yet it is sixteen years since my first attack.

The clinical history and a careful and thorough study of Sir James Mackenzie's heart made at his request were published last year by Dr. David Waterston[5] in the *British Heart Journal*. In the letter written four months before he died Mackenzie said, "All this means that my coronary

arteries are slowly but surely becoming occluded." The autopsy proved the correctness of this statement.

To my personal recollections and to this collection of letters I add in conclusion the fine appreciative sketch of this great man by the one whose name is closely united with his in the development of the clinical pathology of the heart. In a memorial tribute that appeared in the *British Medical Journal,* Sir Thomas Lewis[6] said:

> It was in 1908 and shortly after he migrated to London from his old home and practice at Burnley that I first came to know Mackenzie personally. While it was never my privilege to work under his supervision, yet he extended to me, though many years his junior, a friendship which soon became intimate and highly prized. I found in him during these years before the war, when we were in almost daily and personal communication, a man whole-heartedly devoted to the search for the knowledge of disease, and eager, most eager to impart his spirit and conceptions. He was an exceptionally vigorous and strong personality, intolerant of statements founded on tradition, trenchant and acute in criticism, rich in personal experience, combative in argument, but open nevertheless to conviction on all questions without reserve. He saw, as few or none of his day saw, where clinical knowledge ends and ignorance begins, and never hesitated to define the limits of his knowledge; and he was the first authority in clinical medicine on whose lips I frequently heard the words, "I don't know." To him diagnosis, the affixing of a temporary label, gave little satisfaction; his patient still contained his problem or problems. Mackenzie's mind could not rest on the known, but turned incessantly at each and every hour of the day to the unknown, and in perceiving and defining the unknown he displayed a masterly power. To know Mackenzie intimately was to imbibe independency of thought; none could go to him seriously to discuss, and, surviving the brusque shocks of that first interview, return without a growing inspiration and stimulus. For he possessed a gift of stimulating others in unusual degree.
>
> As a man he was hard headed and warm hearted, quick in temper and in sentiment, genial and hospitable, possessed of an invigorating, blunt humor. Schooled by long experience in the sensibilities, reservations, obstinacies and frailties of patients, he was an astute and shrewd physician, who rarely failed to inspire an unlimited and merited confidence.
>
> This briefly of his practical work as I knew it; as a bedside investigator he ranks in my judgement as the first of his time; he has gone from us to hold a place in the history of British medicine by the side of Sydenham, Stokes, Graves, Addison and Bright, and he will live in memory as not the least of such men.

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TRANSURETHRAL ELECTRORESECTION AS OPPOSED TO PROSTATECTOMY*

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A DISCUSSION of the relative merits of two operations, entirely different in principle yet both designed to accomplish the same result, should be based on a consideration of the pathologic condition for which relief is sought. This is particularly true when obstruction at the bladder neck is the subject of discussion, for such obstruction may be caused by widely different processes.

Randall,[1] in a study based on the autopsy findings in 312 patients with prostatic obstruction, found 17 carcinomas, 57 fibrous bars, 31 glandular bars unaccompanied by lateral-lobe hyperplasia, and 207 cases in which hypertrophy of the lateral lobes existed alone or in combination with one of the preceding conditions.

A classification of the types of prostatic obstruction such as Randall has presented is of primary importance in any discussion of transurethral resection as compared with prostatectomy. Obstructive conditions at the bladder neck are of two types: the enucleable and the nonenucleable. Carcinomas, fibrous bars and glandular bars unaccompanied by lateral-lobe enlargement, which were found in 33 per cent of Randall's series of bladder-neck obstructions, do not lend themselves readily to enucleation, as anyone knows who has attempted to remove them by this method.

Hypertrophied lateral lobes, on the other hand, may be cleanly and easily removed, through either suprapubic or perineal approach, by the simple process of breaking through the thin mucosa of the prostatic urethra at the point where it passes from the projecting lobe onto the roof of the urethra, and sweeping the finger along the line of cleavage between the hypertrophied mass and the prostatic capsule. This leaves a smooth, bowl-shaped cavity; its wall consists of compressed pros-

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tatic tissue 2 or 3 mm. thick, and at the upper and lower poles it narrows sharply to form the entrance and exit of the prostatic urethra (Fig. 1).

That it might be possible to relieve bladder-neck obstruction of the fibrous type by transurethral methods has long been known, and Riba[2]

FIGURE 1. *Large Prostate with Easily Enucleable Lateral Lobes: Lateral lobes partially enucleated.* (*Reproduced from* Surgical Pathology of Prostatic Obstructions[1] [p. 59] *by permission of the publisher.*)

has written a good historical review of the subject. One hundred years ago Mercier[3] devised an instrument for the excision of bars at the vesical neck. Bottini[4] in 1874 developed for this purpose an instrument resembling a lithotrite, the male blade of which was heated by a galvanic current. In 1909 Young[5] introduced his "cold punch," which Caulk[6] later modified by the addition of a cautery blade and a system of lenses.

Stern[7] succeeded in applying high-frequency current to the transurethral removal of bladder-neck obstructions. His instrument was improved by Davis,[8] who in 1931 reported 200 transurethral resections. The Stern–Davis resectoscope was superseded by the McCarthy[9] resectoscope which has been the instrument most widely used in this country. A wire loop, set at right angle to the long axis of the instrument, is charged with a high-frequency current that enables the loop to cut through tissue and to coagulate as it cuts. The operator moves the loop backward and forward by means of a lever, and can change the character of the electric current by means of a foot switch.

The Mayo Clinic has employed a different principle in transurethral resection; the obstructing tissue is removed with a cold punch, and the electric current is used only for coagulating bleeding points. This principle is sound, I believe, and in the early days of resection, when tissues cut by the McCarthy resectoscope were often considerably "overdone," it constituted a distinct advantage in favor of the cold punch. Recent developments in high-frequency machines have given us a current that cuts with very little coagulation, whereas the Thompson[10] resectoscope used at the Mayo Clinic

FIGURE 2. *A Moderate-Sized Solitary Subcervical Hypertrophy (Middle Lobe) Suitable for Transurethral Resection.* (*Reproduced from* Surgical Pathology of Prostatic Obstructions[1] [p. 135] *by permission of the publisher.*)

has so small a field of vision that the operator accustomed to the magnified view of the bladder neck given by McCarthy's Foroblique Lens finds the Thompson instrument almost impossible to use.

For the management of those types of bladder-neck obstruction that are not readily enucleable, transurethral resection is admittedly the best method. One exception should be made; in certain early carcinomas, the total removal of prostate, vesicles and bladder neck as described by Young[11] offers a fair chance of cure, whereas re-

moval of the obstructing tissue by the resectoscope leaves behind that portion of the gland, the posterior lobe, in which from 75 to 80 per cent of prostatic cancers have their origin. Space does not permit the presentation of arguments in support of this rather dogmatic statement, but it is made on the basis of my experience with over 70 total perineal prostatectomies.

Although almost all urologists are in agreement as to the value of resection in nonenucleable obstructions, there is wide divergence of opinion as to its place in the removal of lateral-lobe hyper-

FIGURE 3. *A Fibrous Median Bar, Not Enucleable but Readily Removed by Urethral Punch or Resection.* (*Reproduced from* Surgical Pathology of Prostatic Obstructions[1] [p. 201] *by permission of the publisher.*)

trophies. Most writers agree that small hypertrophies — let us say those not weighing over 20 gm. — may be sufficiently well removed by resection to promise a good result. When the larger hypertrophies are concerned, there is a parting of the ways. Some operators contend that practically any prostate can be resected, although two or more sessions may be necessary. Very few can remove over 50 gm. in an hour, and the leading advocates of resection warn against prolonging the operation beyond this time. Other operators believe that hypertrophies of more than 25 or 30 gm. can be removed more cleanly, more rapidly and even more safely by open operation.

In the early days of resection, surgeons were amazed to find that great relief of obstruction often followed the removal of a few grams of tissue from the bladder neck. This was because the early cases were largely in the nonenucleable class. As larger prostates were attacked, it was learned that simply boring out a channel was not enough; incomplete removal of hypertrophied lobes often resulted in the extrusion into the urethral lumen of small adenomas. These sloughed, bled or obstructed urination. Recently leading resectionists have changed the name of this operation from "transurethral resection" to "transurethral prostatectomy"; they maintain that it is possible as well as essential to remove by transurethral methods the same amount of tissue that would be removed by enucleation.

I do not doubt that a few of the most skillful can approximate this objective, but the technical difficulties are many. The prostatic capsule is 2 or 3 mm. thick; to stop the process of resection at exactly the right depth all over the considerable area filled by good-sized hyperplastic lobes is practically impossible. If one leaves too much tissue, the operation may have to be repeated; if one cuts too deeply, the capsule is perforated and extravasation may result. Yet admittedly the operation is inadequate unless this almost impossible feat is accomplished. Actually, I believe, good clinical results are often obtained even if a considerable layer of hypertrophied tissue is left; this must be so, because we see many good results. The fact remains that the goal of this operation is practically unattainable.

Not so with open prostatectomy; as has been already pointed out, the removal of all the hyperplastic area is easily accomplished by following natural lines of cleavage. Why, then, is transurethral resection employed for those patients whose prostates are well suited for enucleation? The outstanding argument in favor of resection is its allegedly low mortality. In comparison with the mortality of suprapubic prostatectomy, this argument is well founded, but in comparison with that of perineal prostatectomy, it has no basis in fact. Johnson and Burns,[12] from collected series of statistics, found that in 4837 suprapubic operations the death rate was 12.4 per cent, whereas in 4370 perineal operations it was 3.3 per cent. Chetwood[13] collected 27,000 cases of transurethral resection in which the mortality was 3.6 per cent.

It is true that in the hands of a very few specialists in resection the mortality is around 1 per cent, but against this we may set Bugbee's[14] series of 233 suprapubic prostatectomies with a death rate of 0.8 per cent, and Young's record of 2800 perineal prostatectomies with a mortality of 2.8 per cent.

It is a significant fact that among those surgeons trained in perineal prostatectomy, not one, so far

as I know, has abandoned this method in favor of resection except in the nonenucleable type of obstruction.

The management of a condition that is so prevalent as the obstructing prostate cannot be concentrated in the hands of a few operators. Relief of prostatic obstruction will be attempted by practically all the eleven hundred members of the American Urological Association, and by numerous others less qualified for this type of surgery. Orr[16] has shown that the mortality of transurethral resection has been much higher among those operators whose experience with resection has been limited to smaller series of cases.

My own mortality rate with resection versus perineal prostatectomy is definitely in favor of the latter. I have done resections on 200 patients. In the first 100 cases there were 6 deaths; 2 of these were in patients with cancer, 3 were in feeble or elderly persons who were bad risks, and 1 was due to pulmonary embolus. In the last 100 resections there were 6 deaths attributable to the operation, as well as 1 death some weeks after resection from uremia and 1 from pyelonephritis. Three of the operative deaths were due to pulmonary emboli, 1 to upper respiratory infection, 1 to extravasation by the subtrigonal route and 1 to cardiovascular collapse. These figures are deplorable.

In the last 100 perineal prostatectomies that I have done, on ward as well as on private patients, and including several total prostatectomies, there were 2 deaths. One was that of a ward patient who entered the hospital because of cardiac decompensation and prostatic obstruction. His family physician insisted that he have his prostate removed, on the ground that neither cystotomy nor catheter life would be feasible. The patient died of a cardiac relapse four days after operation. I believe that resection would have been less dangerous, even though it had to be repeated, for the position required for perineal prostatectomy adds some load to the circulation. The other death was that of a man who bled more than usual and required transfusion. He made a good immediate recovery, but developed anuria and died twelve days after operation. Autopsy showed a tubular nephritis, considered by the pathologist to be the result of transfusion of improperly matched blood.

Another reason advanced for selecting the transurethral method has to do with the shorter stay in the hospital. One reads of patients discharged in less than a week after operation. In some clinics, this means that the patient is transferred to a nearby hotel, from which he is easily able to attend the outpatient department for daily observation. The possibility that secondary hemorrhage may occur about twelve days after resection makes it unwise to send these patients to their homes in other communities. I believe that the patient should be kept under close observation for at least ten days after operation; it is humiliating to have his own physician telephone to ask what he should do to stop the patient's bleeding. Second resections, which have to be done in 10 to 15 per cent of cases, lengthen the hospital stay.

Following perineal prostatectomy, patients stay in the hospital for two to four weeks. I seldom have one remain over three weeks unless some complication has occurred. Such complications almost always develop before the patient is discharged; the development of serious trouble after that time is rare.

It has been my experience that complete return to normal bladder function is slower in patients after resection than after open operation, although with increased familiarity with resection the results have been better. With cleaner and more complete removal of prostatic tissue, sepsis has been less troublesome. Urethral strictures develop after resection in a small number of patients. Nesbit,[17] to avoid this, advises introducing the resectoscope through a perineal urethrotomy if the urethra is of small caliber.

Both perineal prostatectomy and transurethral resection may be followed by incontinence of urine. That which sometimes follows prostatectomy is almost sure to clear up within three months; I have had among my last 100 patients only 1 in whom control has not been entirely recovered. Although I have had no private cases of resection in which incontinence has persisted for more than six months, Davis[18] tells us that the sale of penis clamps has increased from an average of 100 to 150 clamps for each year of the decade preceding 1928 to an estimated 1600 to 1700 for the year 1938. Since the period distinguished by this tenfold increase in the demand for clamps coincided with that in which transurethral resection developed, one might logically assume that incontinence has flourished *pari passu* with the spread of the latter operation.

Patients frequently ask whether transurethral resection gives as lasting results as does open operation. It is perhaps too soon to answer this question. Orr,[16] from a study of 37 patients questioned or examined five or more years after resection, found that 33 had obtained both objective and subjective relief from their prostatic obstruction. It appears probable that if the resection is thorough, the relief will be as permanent as that after prostatectomy. After resection of a fibrous bar, lateral-lobe hypertrophy may develop later, but

this cannot be considered an argument against resection.

These are, in brief, the advantages and disadvantages of transurethral resection as compared with open prostatectomy. I believe that for the surgeon who does an occasional prostatectomy, the suprapubic method is the safest. For the urologist who does a number of prostatectomies every year, it is well worth while to learn the perineal operation. The technic is really not difficult, although it is often so described. Perineal prostatectomy, and not suprapubic prostatectomy, is the true rival of transurethral resection.

No surgeon should attempt to do resections unless he has first-class equipment, which costs from eleven hundred dollars to twelve hundred dollars, and a well-trained hospital personnel who can carry out the details of postoperative care. To perform a resection well is far more difficult than to perform a good perineal or suprapubic prostatectomy.

Concerning my own attitude toward resection, I am definitely a selectionist. Approximately 45 per cent of the cases of prostatic obstruction that I see fall into the class for which resection seems the best method. These include the fibrous bars, carcinomas and small lateral-lobe and middle-lobe hypertrophies, and a few poor risks for whom resection seems the safest course. I find that I am much more satisfied if I remove the moderate and large hypertrophies by the perineal route. The operating time is less, complications are fewer, the mortality is lower. When I have finished, I know that the obstruction has been relieved and that I shall not have to tell the patient that he must make another trip to the operating room. There is definitely less mental stress for me, and a more complete and workmanlike job for the patient. Undoubtedly there are many urologists whose attitude toward resection is exactly opposite to mine.

Dr. George Brewster once said to me, "A surgeon should use that type of operation from which he can get the best results." This advice is essentially sound, and should be the criterion in the selection of a method for relieving prostatic obstruction.

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Discussion

Dr. John P. Bowler, Hanover, New Hampshire: The crux of the situation is expressed in the conclusion of Dr. Smith's paper, in which he quotes Dr. Brewster to the effect that the best operation is that from which the surgeon is likely to get the best results; in other words, the point to be emphasized is that if the subject were approached from the point of view of the operator rather than of the operation, it would be clearly grasped. There is no doubt that transurethral resection has increased the armamentarium of the surgeon. In the past five or six years I have performed from a hundred and fifty to two hundred such resections, but I am still uncertain as to the value of this procedure. That mere statement is a condemnation of the operation — as well, perhaps, as of me.

The one advantage of transurethral section is that it has increased the operability of early cases with a small residuum — cases that previously have not been considered acceptable for open operation, but those that are relatively simple and in which there is slight risk.

One of the difficulties from the standpoint of practice is that this procedure has been presented to the general public as a minor operation, which is unfortunate. It has not been so in my cases, and certainly the postoperative care is far more detailed and important than that of the open operation.

I see no advantage in the Nesbit procedure. It is neither one thing nor the other, and the combination of urethrotomy and transurethral section seems to me unsound.

The type of operation is a matter for the operator to decide. Transurethral resection is not a minor procedure. It offers distinct advantages in the increased operability of early cases, and is of special value in malignant cases in which there is nothing to offer the patient but the palliation of obstruction. Most of us have not had so much experience as has Dr. Smith in the total perineal operation, so that we are compelled to resort to resection and x-ray treatment.

Dr. J. Dellinger Barney, Boston: Dr. Smith's paper is a splendid summary of his extremely safe and sane attitude toward the advantages and disadvantages of resection as opposed to open operation, whether perineal or suprapubic.

As happens in so many surgical fields, enthusiasm and lack of judgment have now given way to a temperate consideration of every case encountered. When resection first appeared, it was performed by everyone as a minor

and easy procedure that offered cure for all types of cases. It has now come to be realized that this operation is not always possible, and that even when it is, the results are often unsatisfactory. As a consequence, there is now being practiced a more scrupulous selection of cases for resection.

I now perform resections in 60 to 75 per cent of prostatic obstructions. This is much higher than my former percentage, because as one acquires more skill in the operation one is able to manage successfully cases that five or ten years previously one would not have dared to attempt.

Since resection must often be done in two stages, it subjects the patient to a great deal of unnecessary risk. The patient is frequently old and feeble; he must submit to a second anesthesia and go through a second convalescence, not to mention the mental and psychic excitement involved. This being so, the surgeon, unless he feels assured of success, should have recourse instead to open operation.

As to recurrence after resection, I have had only 1 case, an early one. The patient was a young man in good health; the resection was entirely successful, with no bladder symptoms and a clear urine. This condition lasted for five or six years, when obstruction developed; he finally had 10 ounces of residual urine. I performed a suprapubic operation, and found a large prostate that had probably grown after the resection, largely perhaps because I had not resected much tissue in the first place. I removed the prostate and the patient made an excellent recovery; he has been well ever since.

This operation, therefore, fills a distinct lack in being applicable to the type of prostate that Dr. Smith has shown to be impossible or difficult to enucleate by a perineal operation. It is especially suitable for the cancerous prostates that used to be treated by suprapubic cystotomy, or by a fairly extensive perineal operation, which carried a high mortality and involved a great deal of unnecessary risk. The operation is also admirably adapted to old and feeble patients with small prostates. One can sometimes remove only a little prostatic tissue, yet obtain a perfectly good clinical result, and the patient, who will not live very long in any case, is made comfortable.

As time goes on and surgeons gain wider experience with this operation, they will select cases even more carefully, and will make sure that the procedure selected is the best one for the case in hand and involves the least risk to the patient.

Dr. Fletcher H. Colby, Boston: I differ with Dr. Smith in that I regard transurethral resection as the operation of choice for benign enlargement of the prostate or hypertrophy of the prostate whenever possible.

Ever since seeing my first prostatectomy, I have hoped for some better method of relieving urinary retention. Transurethral resection is perhaps not the answer, but it seems to come closer to it than open operation does.

As Dr. Smith has said, it is necessary completely to remove all hypertrophied tissue to perform a satisfactory operation and obtain a good functional result. This requires skill and experience, but it can be done by transurethral resection as well as by open operation. Postmortem specimens removed after transurethral resection have shown the prostate to be as cleanly and adequately removed as would have been possible with any other method.

No good operation should be condemned because it is technically difficult. Resection offers the patient a shorter period of hospitalization, less postoperative pain and discomfort and at least as low a mortality and as good a functional result as open operation does.

Both perineal prostatectomy and transurethral resection are excellent operations; the latter is one of the outstanding contributions to urology. There is no reason why these two operations should conflict, since prostates that are of such size that they can be removed completely by resection are best so treated, and the others are best removed by perineal prostatectomy. The choice between the operations is really one of necessity, and depends on the operator's ability adequately to remove the prostate. The average hypertrophied prostate weighs about 45 gm., and this amount of tissue can be removed by transurethral resection in a reasonable length of time.

I have been able to determine the size of the enlarged prostate and its suitability for resection more accurately by cystourethrograms than by cystoscopic and rectal examination. Furthermore, their use spares the patient the discomfort and danger of cystoscopic examination.

Incontinence or rectal injury should never result from a properly performed transurethral resection. So far as this hazard of operation is concerned, a recent comparison of transurethral resection and perineal prostatectomy by two outstanding surgeons, Nesbit and Davis, showed that the functional result of the two operations was equal except for some incontinence after perineal prostatectomy.

In New England more has been said against than in favor of transurethral resection. I should like to see this operation as favorably considered here as elsewhere, so that patients would not think it necessary to go to other parts of the country to secure its advantages.

Dr. Richard F. O'Neil, Boston: I have heard many papers on this controversial subject but never one to compare with Dr. Smith's in sequence, clearness and convincingness. My colleagues have said about all that is possible to say on the subject, but I should like to add that we have been a little reluctant to carry out resection as freely in Boston as is done in other parts of the country; this policy is, in my opinion, a sound one.

Dr. Smith (closing): I asked Dr. Colby to discuss this paper because I knew that he represented a different point of view from mine. I suspect that we are not so very far apart, except in our psychologic reactions to resections. He likes to do them and I do not. I get much more satisfaction from an open operation where I can control every step by sight and touch, whereas Dr. Colby probably through his superior skill in the use of the instrument, feels more at home when he is working at the end of the resectoscope. I believe that if one has sufficient experience with these cases, one can become extremely skillful in transurethral resection, as has been demonstrated in certain well-known clinics.

One of those present has said that total removal of the prostate by the resectoscope is possible. This statement was made at a medical meeting in Chicago, whereupon a number of surgeons declared that they had performed prostatectomies on patients on whom the speaker had performed resections. These remarks seemed to me rather cruel, but they did show that the resectionist cannot be sure that he has removed all the obstructing tissue.

DISORDERS OF NUTRITIVE DEFICIENCY AND THEIR TREATMENT*

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THE composite picture that portrays the diseases of a people changes from time to time, just as do the sketches in a fashion magazine. True, a quarter of a century alters the lines in the first hardly as much as a single season alters the second, but the changes come just as surely. Thirty years ago the picture familiar to me in the Southern States was intensified by the high lights of typhoid fever, malaria and hookworm. In the next picture those lights were greatly subdued, and there appeared several ugly splotches made by pellagra. Today, the image is wholly different. As the pellagra splotches are being removed there is to be seen an entirely new coloration, all pervading, but in lighter tones, produced by a new group, the less outspoken forms of the deficiency diseases. Since this picture may confront you in New England, I should like to discuss some of its features.

It has well been said that few greater tragedies come to man than the emotional depression, the dulling of intellect and the loss of efficiency that accompany nutritive failure. This applies not alone to the well-characterized deficiency diseases such as outspoken beriberi, pellagra, scurvy and rickets, but with even greater force to these less clearly defined borderline states. They are of vastly more frequent occurrence.

My own interest in these disorders was first aroused by two experiences. In the effort to apply a modified form of the old Weir Mitchell rest cure to a group of patients who offered a large array of vague complaints, none of which could be related to any known disease, I was often gratified to find that the treatment was highly successful, but with almost equal frequency I was puzzled over the explanation of this success. In addition to rest and to psychotherapy of a sort, these so-called "neurasthenics" were given an abundance of food, in which milk and eggs bulked large, and, even though anorexia was a frequent complaint, it was insisted that the patient eat all that was offered him. The results were sometimes graphic. Nervous stability was restored, pains disappeared, vague discomforts were no longer complained of, and the patient's outlook on life was often greatly improved. It finally became evident that it was the food, not the rest or the attempted psychotherapy, that cured the patient.

The other experience came when Dr. J. B. McLester reported that a significant number of patients coming to the Hillman Hospital with pellagra had been admitted the previous year with a diagnosis of neurasthenia. On further investigation it became apparent that before the skin lesions or other evidences of frank pellagra appear, there is often a preclinical state in which nervous instability and diarrhea are prominent features, and that in such cases the old designation pellagra *sine* pellagra is appropriate. We have made a diligent search for patients of this group, and a number have been found.

The deficiencies from which these patients suffer are almost always multiple. Indeed, frank pellagra, although apparently a disease entity, often presents evidence of more than one type of deficiency. Roughness and redness of the lips with inflamed fissures at the corners of the mouth may tell of riboflavin deficiency, or neuritis with edema may point to lack of thiamin and perhaps of protein. So difficult is it to determine precisely the nature of the deficiency from which the patient suffers that, with more seriousness than humor, there is occasionally recorded the diagnosis of "pellagra with a dash of beriberi." This is true not only of the outspoken disease, but also of preclinical pellagra.

The symptoms of preclinical pellagra include nervous instability, personality changes, mental depression, easy exhaustion, anorexia, vague digestive disorders and a tendency toward diarrhea. Often the tongue is red, or there may be merely a history of glossitis. On the other hand, there may be no symptoms other than anorexia and nervous instability. Any of these symptoms may be absent; instead of looseness of the bowels, for example, there may even be constipation. Untreated, the patient may the following spring develop outspoken pellagra, or without clearly defined symptoms he may for years remain merely in vague ill health. In either case adequate treatment will completely restore health.

Subclinical pellagra is not the only borderline form of nutritive failure encountered. There are

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l. 224
941

many others, and in these sometimes one and sometimes another group of symptoms are seen. Digestive discomforts, with abdominal distention and anorexia, often predominate. Sometimes these are the only symptoms. The patients offering such complaints were formerly called neurasthenics, but it now appears that their disabilities are often genuine, being largely due to loss of muscle tone, which, like the neuritis of similar origin, is dependent on lack of vitamin B_1. Diarrhea sometimes dominates the clinical picture. Many years ago, we first began to see at the Hillman Hospital patients with achlorhydria whose only other evidence of disease was diarrhea. No doubt many of these had pernicious anemia, but not all. Some had early pellagra. The diarrhea of others was apparently nonspecific but was dependent nonetheless on nutritive deficiency. Patients of this last group usually recovered promptly when given an abundant diet, including liberal quantities of milk and eggs. Such patients continue to appear, and although even today their disorder cannot always be identified with any of the well-defined deficiency diseases, if they are given liver extract the diarrhea as a rule disappears.

Of a different type, perhaps, is the occasional patient with achlorhydria and an anemia of nondescript character who tells of one or two copious bowel movements each morning with nausea and, perhaps, profound exhaustion. During the rest of the day he feels well. Sometimes the tongue is red. In the sigmoidoscope the mucous membrane appears smooth and glistening, and in the fluoroscope the large bowel has a smooth, stringy appearance with loss of haustra. This is apparently a mild form of sprue, for large doses of liver extract given intramuscularly are always of benefit.

One of the commonest as well as the most distressing symptoms encountered in the borderline states is mental depression. Many deficiency disorders are accompanied by this symptom, but I have been particularly impressed by two groups of patients in whom mental depression predominates: in the one, nutritive failure is merely a contributing factor; in the other, it is apparently the underlying cause of the depression. As an example of the first group, I have seen a patient with typical manic depressive insanity of many years' duration greatly improved when the faulty dietary habits of a lifetime were corrected and nicotinic acid and thiamin given. Similar improvement has been seen in cases of so-called "involutional melancholia." Patients of the other group may present additional signs of nutritive failure, but as a rule nervous instability and emotional depression are the only evidences of ill health. I have seen patients of this type for whose depression no ready explanation could be found promptly regain their equilibrium and sense of well-being when they were given intramuscular injections of liver extract. Other patients present a symptom complex identical with what is sometimes labeled toxic psychosis. They are confused, disturbed in speech and disorientated, and their gait is often unsteady. They are as a rule users of alcohol, though not necessarily to excess. When they are given thiamin and nicotinic acid, the psychosis, thick speech, and unsteady gait disappear.

Even the disabilities of old age are sometimes due in part to lack of nutritive essentials. An example of this was seen in the case of a charming elderly lady whose complaints of weakness, unsteadiness in gait and unwonted mental depression were at first regarded as the inevitable accompaniment of years. When it was discovered, however, that her tongue had the appearance of raw beef, although no fault could be found in her diet except its frugality, she was given large quantities of yeast, supplemented by thiamin and riboflavin. Immediately the tongue assumed a normal appearance and the patient's former sense of well-being returned. This is not an uncommon experience. In such cases it seems fair to assume that the changes of advanced age have in some way interfered with the absorption and utilization of essential substances. I do not mean to suggest that adequacy in nutrition will prevent old age; far from it. I do make bold, however, to say that if the results of animal experiment can be applied to man, it can be assumed that long-continued nutritive deficiency will hasten the onset of old age, and conversely that an optimal diet observed throughout the greater part of a person's life will postpone senility. What is of even greater interest, such a diet can be expected to prolong the person's period of usefulness.

Vitamin deficiency is not the only cause of nutritive failure. Deficiency disorders are produced just as effectively, though not always in so graphic a manner, by lack of proteins and of minerals. Witness the endemic edema that is due in part to protein deficiency, as is the edema sometimes seen in pellagra. Of similar nature is the puffiness of the ankles exhibited by patients convalescing from a long illness. Even the so-called "toxemia of pregnancy" described by Strauss is apparently due to lack of protein. Here again, if the results of experiments on animals can be applied to man, it may be assumed that lack of protein in the diet will lead to easy exhaustion, loss of stamina and other disabilities; this accords with clinical experience.

Lack of iron is also a potent cause of trouble. I

have been impressed by the frequency of iron-deficiency anemias. It has repeatedly been observed that this type of anemia occurs oftenest in women in the late teens or about the time of the menopause. These are frequently apparently healthy girls and young women who complain only of easy exhaustion, and not always of that. This disease seems to me to be identical with the chlorosis described here and in England forty years ago, but I am under the impression that we see it in the South today more frequently than it is seen in New England. The combined demands of growth and menstruation, and in addition oftentimes a freaky appetite, with a deficient diet are probable causative factors. Another form of iron-deficiency anemia is that described as the idiopathic anemia of middle-aged women with achlorhydria. Many of these patients are chronic invalids who live on a diet deficient in iron. Menorrhagia and bleeding hemorrhoids may also be causative factors. There is reason for believing that in the first group, and possibly in the second group also, difficulties of absorption play an important role.

For the prevention of nutritive failure, a reasonably liberal, well-balanced diet is as a rule sufficient; it is well to emphasize, too, that for this purpose vitamins and minerals should be obtained, not from the druggist, but from the grocer and the dairyman. This is not true, however, in every case, for there are many conditions in which nutritive needs are greatly increased, and the food, therefore, should be fortified with more concentrated substances. These conditions may be physiologic, as in increased exercise and in pregnancy and lactation. At other times the increased demand may be due to illness, as in infectious diseases, hyperthyroidism and many forms of chronic illness. In addition, the possibility of inadequate absorption must be considered. The absence of bile from the intestinal tract, achlorhydria, frequent diarrhea or a history of alcoholism should provide a warning that nutritive substances taken by mouth may not be adequately absorbed. In such cases greatly increased amounts of these substances should be given, or they should be administered parenterally.

The distorted anatomic relations and consequent disturbances of function that occasionally follow a short-circuiting or other operation on the bowel may lead to nutritional failure no matter how abundant the diet. Such a fault can rarely be corrected, but I recently saw this accomplished in a very gratifying manner by means of a second operation. In the effort to prevent deficiency disease, therefore, particularly after a febrile illness or in the presence of gastrointestinal derangement, the diet should be considered from two viewpoints, first in the light of the person's nutritive needs, and secondly in regard to his ability adequately to absorb and utilize all essential substances.

Once, however, the deficiency becomes manifest, the picture changes and the need grows vastly more urgent. Treatment under these circumstances should be governed by three principles, which are as follows.

First, the patient can no longer depend solely on the grocer and the dairyman. Recourse must be had also to the pharmacist, and the missing substances be secured in concentrated form.

Secondly, because the deficiencies under discussion are seldom single, more than one vitamin or other essential substance must as a rule be given. Pellagra, for example, cannot always be cured with nicotinic acid alone; thiamin and riboflavin also are often needed, as well as proteins of good quality. A like condition obtains in many other states of nutritive failure, and for this reason two substances have come into use that are especially suitable, yeast and liver extract. The value of the latter when given intramuscularly has been demonstrated in a number of nutritive disorders, both outspoken and borderline. This, no doubt, is because the liver as the "commissariat" of the body elaborates and stores a number of essential substances. Extracts made from this organ can provide not only the antianemic principle but also other necessary material, and such preparations should not, therefore, be too highly concentrated. Even in such a clear-cut deficiency disease as pernicious anemia the patient often gets a greater "lift" and his sense of well-being reaches a higher plane if he is given the liver extract that carries the broader fractions.

Thirdly, the needed substances must be given in relatively enormous amounts. Before the nicotinic-acid era, for example, it was known at the Hillman Hospital that the daily dose of brewer's yeast that could with maximum benefit be given pellagrins was 180 to 270 gm. (a half pound!). Although 1 mg. of thiamin is regarded as the maintenance dose, it has been found in deficiency states that 20 to 50 mg. daily must be given before clinical improvement is seen, and cases of nerve injury have been reported in which 100 mg. of this vitamin daily were required. The same is true of vitamin C. Whereas 40 to 60 mg. has been estimated as the optimal intake, deficiency states have been reported in which ten to twenty-five times this amount was necessary. Likewise, in the use of liver extract I have found that vastly better results can be obtained if very large amounts

are used; massive doses sometimes bring excellent results when small doses have accomplished nothing. It is difficult to understand the magnitude of this need unless it be that it is due in part to the necessity for replenishing exhausted stores. The physician who would treat deficiency diseases cannot afford to be timid.

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MEDICAL PROGRESS

CLINICAL BLOOD CHEMISTRY IN GENERAL PRACTICE*

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BOSTON

THE extensive use of blood chemistry in clinical medicine was established largely through the efforts of the late Professor Otto Folin,[1] within the memory of the present generation of active practitioners. The value of such procedures to confirm bedside impressions and to follow quantitatively the progress of disease is now unquestioned. Two general abuses, however, have arisen: the abandonment of sound clinical observation and clear thinking in favor of laboratory reports, and the misinterpretation of such data through ignorance of their limitations and of the several factors that together yield a given physiologic concentration. These abuses will disappear only when physicians become better acquainted with the intricacies of human physiology.

To call attention to the possible pitfalls that confront the interpreter of chemical data, this synopsis of common laboratory tests has been formulated. It should be read with the mental reservation that, owing to various physiologic complexities and analytical complications, the statements made below are not over 80 per cent correct.

The constituents of the blood that are commonly used in clinical medicine may be classified arbitrarily as follows: plasma proteins; nonprotein nitrogenous compounds; sugar; lipoids; pigments; calcium and phosphate; bases (cations); acids (anions); and regulators (vitamins, enzymes and hormones). In the summary that follows, only the commonest examples of each of these are cited.

Whole blood versus serum or plasma. Because blood is a two-phase system of cells and plasma, determinations of concentrations in whole blood record necessarily the average of two values, that is, the concentration in the cells and the concentration in the plasma. In general, plasma or serum values are preferable, because they reflect more directly the true *milieu interne*. Moreover, differential permeability complicates the problem. Thus human red blood cells probably contain no calcium; if a calcium estimation were performed on whole blood, therefore, the answer would record the net effect of a 45 per cent fraction (cells) containing no calcium, plus a 55 per cent fraction (plasma) containing 10 mg. per 100 cc. of calcium. Thus the whole blood calcium would be 5.5 mg., but it would vary with the hematocrit reading.

The differences are even more confusing when chloride or carbon dioxide is investigated, because these substances may shift from plasma to cells, depending on circumstances. Moreover, the variation in the normal range may lead to serious misunderstandings. For example, a recent diagnosis of Addison's disease was falsely made because a *whole-blood* value for chloride of 80 milliequiv. per liter (normal) was reported to a clinician who was accustomed to think in terms of the normal *plasma* value of 108 milliequiv. Similarly, a *plasma* carbon dioxide combining capacity of 70 vol. per cent was misinterpreted as evidence of alkalosis by a clinician who was accustomed to think in terms of the normal *whole-blood* value of 48 vol.

With rare exceptions, it is advisable to avoid the use of whole blood, by employing plasma for all determinations except inorganic electrolytes, for which serum may be used. At the present time, however, whole blood is used for many purposes, so that this synopsis will describe values for it in those cases in which it is commonly employed.

PLASMA PROTEINS

Plasma proteins are ordinarily determined by some modification of the Kjeldahl procedure. After oxidation and digestion the ammonia nitrogen may be determined either by alkalimetric titration or colorimetrically after nesslerization. Reliable methods are given by Folin.[1] In my[2] progress report for last year, modern revisions of protein frac-

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tionation were discussed. The fractions described here, however, represent the old-fashioned partitions still in common use.

Normal values usually range from 6.5 to 7.5 gm. per 100 cc. Rarely, values of 6.3 to 8.0 gm. are found under physiologic circumstances. The protein may be subdivided as follows: albumin, the value for which is usually between 3.8 and 4.4 gm.; and globulin, the value for which is usually 2.2 to 3.4 gm. The value for fibrinogen is usually under 0.6 gm. and is ordinarily included in the globulin fraction. The albumin-globulin (A:G) ratio, therefore, is usually between 1.4 and 2.2.

Low values for total protein are encountered in parenchymatous Bright's disease (the so-called "nephrotic" syndrome), in malnutrition and in infections. In *edema* the critical average values that herald the onset are for total protein 5.0 to 5.5 gm. per 100 cc., and for albumin 2.5 gm.

High values are commonly found in the marked dehydration that accompanies vomiting and diarrhea. Thus in cholera the total protein may reach over 11 gm. per 100 cc. Values over 12 gm. are not uncommon in multiple myeloma. In lymphogranuloma inguinale some elevation of protein is also common. The globulin fraction tends to be high in hepatic inflammation but usually falls after extensive liver damage. Among the infections, kala-azar commonly produces high globulin values.

Nonprotein Nitrogenous Compounds

Blood Urea Nitrogen

The value for blood urea nitrogen may be determined gasometrically by measurement of the nitrogen evolved after treatment with hypobromite. It is also very conveniently estimated by the determination of ammonia after treatment with the enzyme, urease. Reliable methods are given by Peters and Van Slyke.[3]

Normal values are usually between 9 and 14 mg. per 100 cc. Rarely, values of between 5 and 23 mg. are found under physiologic circumstances. This variability is usually due to changes in normal nitrogen metabolism. For example, Priestley and Hindmarsh[4] found that when the urinary nitrogen reached 11.2 gm. per twenty-four hours the blood urea nitrogen was 11.3 mg. per 100 cc.

Low values are frequently found after diuresis because urea is swept out with body water. The values tend to be low in pregnancy and in acute yellow atrophy of the liver. Because a high-carbohydrate diet spares protein metabolism, the normal range may drop 40 per cent when carbohydrate is forced.

High values are found in dehydration, in primary renal insufficiency and in renal insufficiency due to congestive heart failure.

Special tests. Two clinical function tests involve the determination of blood urea nitrogen. The urea-clearance test of Van Slyke[5] relates the urinary urea to the blood urea by determining the volume of blood theoretically cleared of urea in one minute. The Mosenthal index[6] is the ratio of blood-urea nitrogen to total nonprotein nitrogen multiplied by 100. The upper limit of normal is 44. Values above 80 suggest strongly Bright's disease and impending uremia. A normal ratio with high total nonprotein nitrogen suggests that primary renal insufficiency is not present.

Blood Nonprotein Nitrogen (Total)

After precipitation of blood proteins, the total nitrogen in the filtrate is estimated after Kjeldahl's digestion. The ammonia so formed is commonly determined colorimetrically after nesslerization. Reliable methods are given by Folin.[1]

Normal values usually range between 25 and 35 mg. per 100 cc., rarely between 25 and 40 mg. Occasionally, a normal person on a high-protein diet may show 45 mg. The total nonprotein nitrogen represents the sum of nitrogen moieties contributed by urea, aminoacids, uric acid, creatine, creatinine and the undetermined nitrogenous material in the blood filtrate. The nonprotein nitrogen concentration is higher in the corpuscles. In the plasma, it is ordinarily only 18 to 30 mg. per 100 cc., that is, approximately twice the blood urea nitrogen. The discrepancy between corpuscles and plasma is due largely to nitrogenous material of unknown composition; consequently, plasma determinations are much to be preferred. In general, considerable variations of nonprotein nitrogen are caused by alterations in urea nitrogen, in the undetermined nitrogen fraction, or in both. Blood nonprotein nitrogen reflects the balance between protein catabolism and urinary elimination. Consequently, there are considerable diurnal variations that bespeak the necessity of determining fasting values. Retention of water or diuresis will also change the nonprotein nitrogen.

Low values are found in starvation, in cachexia and to a certain extent in pregnancy. Unlike blood urea nitrogen, the total nonprotein nitrogen is ordinarily not affected in moderate hepatic disturbance.

High values are found in the characteristic azote-

mia of nephritis, in which values ranging from 100 to over 200 mg. per 100 cc. are common in the terminal stages or during acute exacerbations. Poisoning from mercury and uranium, as well as that from certain drugs, has much the same effect. One may find a high nonprotein nitrogen in dehydration such as that associated with heat cramps, after severe burns, including x-ray necrosis, in the crises of hyperthyroidism, in hyperparathyroidism of marked degree, in advanced hepatic cirrhosis and in gastrointestinal obstruction associated with repeated vomiting or after prolonged severe diarrhea, as in cholera. Even such common disturbances as chronic passive congestion, surgical shock, severe fevers, acute infections, diabetic coma and, possibly, uncomplicated gout lead to some elevation. Lack of salt, particularly in the crises of Addison's disease, is associated with azotemia. Azotemia also accompanies the hepatorenal death found in Weil's disease.

. 224
941

Blood Uric Acid

The value for blood uric acid is ordinarily determined colorimetrically. A convenient method is that of Folin.[7] Uncertainty still exists as to how uric acid is distributed between cells and plasma, and for this reason it is probably much better to use serum.[8]

Normal values are, for blood, 2.0 to 4.5 mg. per 100 cc., and for serum 3.0 to 5.0 mg. These values vary considerably in different laboratories, according to the technic used. In general, any single value of 6 mg. or above should be repeated, even though there is no clinical indication of gout. Normal values are affected somewhat by meals, especially those high in fats and nucleins.

Low values are not striking, but tend to occur after such medication as thyroid, cinchophen or colchicine and after diuresis induced by calcium chloride.

High values may be produced by fasting, especially in children, in whom a four-day fast may cause an elevation up to 10 or even 12 mg. per 100 cc. On the other hand, this condition may be relieved by the feeding of carbohydrate, protein or aminoacids. The feeding of thymus (true sweetbread) may cause a moderate rise. In gout (podagra), elevations in serum uric acid concentration from 5 to 11 mg. per 100 cc. occur in the majority of cases if repeated determinations are made at appropriate critical times.[8] Moderate elevations are common in leukemia, in advanced chronic nephritis and in polycythemia. Pneumonia may cause a temporary rise, and even severe exercise may increase the value about 1 mg. per 100 cc.

Blood Creatinine

The value for blood creatinine is commonly determined by the colorimetric method of Jaffe, which involves the use of alkaline picrate. A reliable modified method is that of Danielson.[9] There is an academic dispute whether in vivo creatinine exists as such or in the form of a chemical precursor. This material is distributed equally between cells and plasma. Its concentration is more constant than that of any other nitrogenous component of the blood. It is essentially unaffected by age, diet, exercise or pregnancy.

Normal values range from 1.0 to 1.8 mg. per 100 cc.

High values, up to 5.0 mg. per 100 cc., are common in chronic nephritis. Indeed, most clinical values over 2.5 mg. are due to nephritis. Above 10 mg. the prognosis is ordinarily very poor, and a value approaching 18 mg. implies imminent death. In urologic conditions producing obstruction low in the urinary tract, the creatinine tends to be but slightly elevated, even when the blood urea nitrogen is high. This point is of diagnostic interest in prostatism, urethral stricture and cancer of the bladder.

Sugar

Blood Glucose

The value for blood glucose is ordinarily determined colorimetrically by one of the two Folin methods involving either an alkaline copper reduction[1] or the ferricyanide reagent.[10] Of course, many other reliable reagents and methods have been described, such as the Somogyi[11] or Shaffer-Hartmann[12] titration methods. The corpuscles contain much reducing substance that is not glucose. For this reason the use of unlaked blood was introduced by Folin.[13] Probably fresh plasma or serum is preferable from a chemical standpoint. In general, blood glucose tends to be destroyed rapidly unless careful measures are taken to preserve it.

Normal values of about 70 to 100 mg. per 100 cc., fasting, are obtained by the methods mentioned. Over 130 mg. is probably abnormal. For whole blood, between 20 and 30 mg. of the reducing substance is probably not glucose. In the cells as much as 41 to 51 mg. of false reducing value is found, whereas only 7 to 13 mg. is present in plasma.

Low values occur in starvation, in pituitary hypofunction, in exhaustion, for example, during a marathon race, and in Addison's disease. In severe liver necrosis due to phosphorus or chloroform poi-

soning and in acute yellow atrophy of the liver, severe hypoglycemia may cause fatal convulsions. In tumor of the pancreas, or hyperfunction such as may follow the assimilation of glucose, marked reduction of blood sugar may occur.

High values are found in excitement, fear, cold and asphyxia (especially in carbon monoxide poisoning) and after brain injury. These conditions represent reactions of the sympathetic nervous system, as described by Bernard and also by Cannon.[14] Hyperglycemia after meals is common in hyperthyroidism and may simulate closely true diabetes mellitus. Even in normal people, it is said that so-called "alimentary hyperglycemia" may lead to glycosuria. A variety of nondescript disturbances may cause intermittent glycosuria. In the dehydration of children and in eclampsia these may be accompanied by temporary hyperglycemia, but in uncomplicated renal injury the blood sugar is usually normal. The differentiation of various clinical types of glycosuria is well discussed by Joslin and his associates[15] in the well-known monograph on diabetes mellitus.

Glucose-tolerance curves. This procedure has assumed increasing importance since the recognition of the role of the pituitary gland in diabetes, as described by Houssay.[16] The simultaneous administration of insulin is now used as a special form of differential functional test, as discussed by Himsworth.[17] It should be remembered that venous blood tends to be lower than arterial blood in the normal postabsorptive patient, whereas the reverse may be true in diabetes.

Lipoids

Blood Cholesterol

The value for blood cholesterol is usually determined colorimetrically by the acetic anhydride reagent,[18] but it is widely recognized that this method includes other substances. The extent of the error depends on the details of the manipulation involved, so that the normal range varies a great deal with local conditions. For research purposes, precipitation by digitonin[19] is sometimes preferred, despite the high cost of the reagent. The total cholesterol may be divided into two portions, that is, the free and the esterified. Cells and plasma contain the same concentration of total cholesterol, but in the fasting state the red cells contain practically no cholesterol ester. In the normal plasma, free and esterified cholesterol are present in constant and nearly equal proportions.

Normal values in many laboratories range from 140 to 170 mg. per 100 cc., rarely from 100 to 230 mg., for total cholesterol.

Low values are found in prolonged starvation, in cachexia, in scurvy, in severe infections and in certain anemias. In infancy, values as low as 50 mg. per 100 cc. are not uncommon. In hyperthyroidism, cholesterol tends to fall as the basal metabolism rises, but there is no reliable standard by which to evaluate a single determination in the individual patient.

High values, such as 300 mg. per 100 cc. or over, are found in pregnancy, myxedema and the so-called "nephrotic syndrome." Cholesterol may be increased in diabetes, but this is not invariable. After a meal there is usually a slight rise in total cholesterol, and after the ingestion of meat this rise may be prolonged. In liver disease, especially when icterus is present, cholesterol is elevated. The ratio of esters to free cholesterol is characteristically low in parenchymatous disease of the liver.

Pigments

Plasma Bilirubin

The value for this pigment is usually determined by van den Bergh's colorimetric reagent. A convenient modification is that of Rhamy and Adams.[20]

Normal values range from 0.25 to 0.6 mg. per 100 cc., corresponding to an icteric index of less than 8. One van den Bergh unit equals 0.5 mg. per cent bilirubin. It should be noticed that the quantitative van den Bergh procedure does not reflect the qualitative type of jaundice.

High values are now rarely found in pernicious anemia, although a moderate elevation was formerly common, that is, 1 to 2 mg. per 100 cc. or an icteric index of 20 to 25. Somewhat higher values often occur in hepatic cirrhosis. In hemolytic anemia the increase in bilirubin varies with the disease. In obstructive jaundice or in acute yellow atrophy extremely high values are found, for example, over 40 mg. per 100 cc., corresponding to an icteric index well over 100. As a rough approximation, skin pigmentation occurs at 4 van den Bergh units, equaling 2 mg. per 100 cc. or an icteric index of 20.

The qualitative van den Bergh test is now thought by many investigators to be of dubious value in most cases. It rests on the principle that normal blood plasma contains colloidal bilirubin, whereas normal bile contains the pigment after detachment from its colloid carrier. The qualitative test should not be confused with the quantitative procedure used to determine total bilirubin. Characteristic findings in different types of jaundice are summarized in Table 1. It should be mentioned that obstruction due to stone in the common bile duct is rarely complete when subjected to such quantitative evaluation. On the other hand, cancerous obstruction is frequently complete.

Calcium and Phosphorus

Serum Calcium

The value for serum calcium is usually determined by titration (with permanganate or with acid) after precipitation as calcium oxalate. Obviously, oxalated plasma cannot be used for this determination. A reliable method is that of Fiske and Logan.[21]

Normal values range from 9 to 11 mg. per 100 cc., that is, a concentration of 5 milliequiv. per liter (2.5 millimolar). Ordinarily, 3 to 5 mg. per 100 cc. of this amount is bound to protein. Other things being equal, calcium falls as inorganic phosphate rises, and conversely, calcium rises with increase of plasma protein. These two trends should be considered in evaluating the virtual normal in any given case. Mathematically, they may be expressed more precisely by the following equations:

> At pH 7.4, calcium (mg. per 100 cc.) = 0.556 protein (gm. per 100 cc.) + 6; or, for adults, calcium (mg. per 100 cc.) = 0.556 protein (gm. per 100 cc.) — 0.255 phosphorus (mg. per 100 cc.) + 7.

This last equation refers to inorganic phosphate, expressed in terms of its inherent phosphorus.[22]

Low values, for example, 4 mg. per 100 cc., are found in severe hypoparathyroidism. In nephritis the calcium drops as phosphate retention ensues or when malnutrition produces low plasma protein. In Gee's steatorrhea (adult celiac disease) excessive loss of calcium soaps by the bowel may reduce the serum calcium to well below 7 mg. Two types of osteomalacia are recognized. In the first, calcium is little reduced but phosphate is subnormal; in the second, calcium is low and phosphate is normal to slightly increased. The latter type occurs much more commonly. Ordinarily, clinical tetany is likely to occur with values below 7 mg. per 100 cc. and is imminent below 5 mg.

High values may occur secondary to increased plasma protein, as in multiple myeloma. In hyperparathyroidism, increases are found up to a critical level of 20 mg. per 100 cc. Artificial hypervitaminosis D may in extreme cases push the level up to 40 mg. for short periods, apparently without marked deleterious effect. The synopsis in Table 2 is intended simply to give a rough idea of the combined blood findings in tetany. Exceptions to the findings recorded in the table are given by Peters and Van Slyke.[3]

In parathyroid disease the usual or characteristic combination of findings is as follows: In hypoparathyroidism calcium is low, phosphate is increased, calcium excretion and phosphate excretion are both diminished, serum phosphatase (see below) is normal, and tetany is present. In hyperparathyroidism, on the other hand, calcium is elevated, phosphate is diminished, both calcium and phosphate excretion tend to be increased, serum phosphatase is often increased, and there is neuromuscular hypotonia.

Normal values for serum calcium are the rule in Paget's disease (osteitis deformans) and in hyperthyroidism. This is true in spite of the abnormally high calcium elimination during the active phases of each of these disturbances.

Table 1. *Pigment Metabolism in Jaundice.*

Diagnosis	Plasma			Urine†				Stools†	
	Colloidal bilirubin	Bile pigment	Urobilinogen	Colloidal bilirubin	File pigment	Urobilinogen	Urobilin	Combined urobilin and urobilinogen	Urobilin	Combined urobilin and urobilinogen
								mg.		mg.
Normal subject.....	+		0–trace	0	0	+	+	0–4	+++	40–280
Hemolytic jaundice ...	++++	0	Trace	0	0	Often sl. +		1–10	++++	300–1800
Crisis or complication	++++	+	Trace		+	++++	+++	10–300		
Hepatogenous jaundice.	?+	+++			+++	++*	++ to ++++	4–200	++*	10–300
Complete obstruction of common bile duct .	+	++++			++++	0	0	0	0	0–5

*Except in acholic stool period.
†Data represent 24-hour periods.

Table 2. *Blood Findings in Tetany.*

Type of Tetany	Serum Calcium	Blood Bicarbonate	Plasma pH	Serum Phosphate as P
Parathyroid	Low	Normal	Normal?	Increased
Gastric	Normal	Increased	Alkaline	Normal
Hyperpneic	Normal	Low	Alkaline	Normal
Alkaline	Normal	Increased	Alkaline	Normal
"Infantile"	Low	Normal	Normal	Increased?

Serum Phosphate

The value for the phosphate ion ($H_2PO_4^-$) is ordinarily determined colorimetrically with a phosphomolybdate reagent: the result is expressed in terms of the inherent phosphorus. A convenient method is that of Fiske and Subbarrow.[23] The cell content is in dispute.

Normal values for adults' serum range from 2 to 5 mg. per 100 cc.; for infants' serum, from 4 to 7 mg. Although inorganic phosphate is the type of phosphorus compound ordinarily referred to in the clinical literature, occasional reference will also be

found to acid-soluble phosphorus, for which normal ranges are as follows: in adults the cells contain 44 to 82 mg. per 100 cc. but the serum only 2.5 to 5.5 mg.; in infants the cells contain 43 to 70 mg., and the serum 4 to 8 mg. This acid-soluble phosphorus fraction exists in addition to the inorganic phosphate commonly referred to. In all cases the values refer to inherent phosphorus.

Low values for inorganic phosphate are found in the common variety of rickets and probably in the late rise characteristic of advanced, terminal hyperparathyroidism. Of the two known types of osteomalacia, that with low serum phosphate is found occasionally. Forced breathing may reduce inorganic phosphate to 1 mg. per 100 cc. of phosphorus. Likewise, insulin and adrenaline cause a fall.

High values are found in hypoparathyroidism, in acidosis induced by carbon dioxide and after the administration of pituitrin. In chronic nephritis inorganic phosphate retention has important prognostic significance. At 8 mg. per 100 cc. the condition becomes critical, and at 20 mg. death is to be expected.

Because phosphate is intimately connected with the chemistry of carbohydrates, fluctuations in carbohydrate metabolism frequently alter the concentration of serum phosphate. It is interesting that despite the marked clinical correlation of high plasma phosphate with low serum calcium, the onset of tetany is not directly related to the phosphate except through pH and calcium. Indeed, there is scientific evidence that the local concentration of carbon dioxide in the tissues, not the calcium or the reaction, is the final precipitating factor in tetany.[24]

Bases

Serum Total Base

The serum total base represents the sum of the extracellular blood bases: sodium, potassium, magnesium and calcium.[25] It is often determined electrolytically, by the method of Consolazio and Talbott,[26] or, more simply, by titrimetric determination of the total inorganic sulfate equivalent to it, by the method of Stadie and Ross.[27] Obviously, one cannot use sodium oxalate as an anticoagulant for plasma. A convenient method for determining the value of sodium is that of Butler and Tuthill[28]; for determining the value of potassium, that of Fiske and Litarczek.[29] Because different cations have different equivalent weights, it is preferable to speak of their concentrations in terms of milliequivalents per liter of serum or, more scientifically speaking, per liter of serum water. With this reduced terminology, the various cations listed below can be added together and considered in toto.

For the uninitiated, the following analogy may clarify the reason for the use of milliequivalents in summating the concentrations of various electrolytes: on a farm it is possible to specify the total number of animals, even though rats, sheep, cows and horses have quite different individual weights.

Several important physiological principles should be remembered in considering the concentration of the various serum bases. The concentration of the total base and of the constituent cations tends to be maintained even under considerable stress, so that the osmotic pressure of body fluids remains nearly constant. Moreover, the liquid outside of cells is in equilibrium across the cell membrane with the cell sap, which has the same concentration of total osmotically active ions as the serum with which it is equilibrated. This is true, of course, only when the concentrations are expressed in terms of equivalents of ions per kilogram of water, because 100 cc. of cells contains only 75 to 85 gm. of water, whereas serum contains 92 gm. of water and transudates 99 gm. Thus, per kilogram of total cell substance (75 per cent water), there are only 112 milliequiv. of total base, as compared with 148 milliequiv. per kilogram of serum. In addition, there is the slight complication that protein itself can bind base.

In general, the organism retains water and base simultaneously to form a sort of Ringer's solution. If extracellular fluid is gained, sodium is retained, but if the new fluid is intracellular, potassium is retained. Individual anions, for example, chloride, are subject to great change, although the summated anions must approximately balance the total base. On the other hand, total base and total anions do not vary greatly, and even individual bases change relatively little. Alterations in metabolism of total base, therefore, are compensated for by expansion or shrinking of the tissue spaces, which serve as a volume buffer, as described by Gamble.[30]

TABLE 3. *Serum–Water Concentrations of Common Cations.*

CATION	SERUM *milliequiv. per liter*	CELLS *milliequiv. per liter*
(Na^+)	154	0?
(K^+)	5	170
(Ca^{++})	5	0?
(Mg^{++})	3–	4
Totals	167	174

Normal values range usually from 160 to 168 milliequiv. per liter of serum water, and ordinari-

ly sodium accounts for over 90 per cent of the total base. In Table 3 the concentrations of the common cations are given in milliequivalents.

Because the total number of positive charges in solution must approximately equal the total number of negative charges, it is evident that the total base must approximately equal the total anions.

TABLE 4. *Component Cations (Total Base) and Anions (Total Acid) in Normal Serum.*

	Total base = total acid																						
	Sum of positively charged ions (cations) = sum of negatively charged ions (anions)																						
	Na^+	+	K^+	+	2 Ca^{++}	+	2 Mg^{++}	=	Cl^-	+	HCO_3^-	+	f^* × protein$^-$	+	$H_2PO_4^-$	+	R^-†						
Expressed as milliequiv. per liter:	142	+	5	+	5	+	2	=	105	+	25	+	17	+	2	+	5	=	154				
Expressed as mg. per 100 cc.:	327	+	19	+	10	+	2.4		374				f^* × 7000	+	3.1								
Expressed as vol. per cent:													48										

*The factor, *f*, by which the protein concentration is multiplied expresses the net capacity of the combined plasma proteins to bind base at pH = 7.4

†Sulfate + organic acid radicles.

Note that the value for the total base is only about 154 milliequiv. per liter for serum, as compared with 167 milliequiv. for serum water (Table 3). This is true because only 92 per cent of serum is water. The values for serum water and cell water, that is, 167 and 174 milliequiv. respectively, also differ slightly.

This will be clear from the equations listed in Table 4, which give the typical normal values for the individual components.

Low values for serum water, that is, a fall of 10 per cent or 15 to 20 milliequiv. per liter, may occur in severe burns, in marked pyloric stenosis or in terminal nephritis. Representative values in nephritis with edema might be 142 to 156 milliequiv., as compared with 150 to 160 milliequiv. without edema. Because the kidney fails to conserve base in chronic glomerulonephritis, late values may be 139 to 149 milliequiv. Similarly, in severe sweating causing heat cramps, the total base may fall to 140 milliequiv., of which sodium supplies 130. In the edema of malnutrition, as in diabetes, the total base may occasionally fall to 130 milliequiv. Of course, the foregoing values all represent concentrations per liter of serum water. Low values are also found in Addison's disease, in Simmonds's cachexia, in major gastrointestinal upsets and in acute poisoning with bichloride of mercury. Even the severe sweating of acute fevers, for example, pneumonia, may induce a definite fall. Of specific interest is the low potassium in familial periodic paralysis.

High values are found in x-ray nephritis, when potassium may increase severalfold. It increases in Addison's disease, for which reason the total base often fails to fall appreciably despite a marked drop in the sodium. High potassium has been described in intestinal obstruction and in acute attacks of Ménière's disease.

Acids

Plasma Chloride

The value for plasma chloride is usually determined by titrating as silver chloride. A convenient method is that of Van Slyke and Sendroy.[31] Red cells show only half the concentration of plasma, partly because of Donnan's equilibrium.[32] Chloride is the most abundant electrolyte and crystalloid constituent of the blood. In sweating, diuresis or a low-salt diet, chloride tends to run parallel with sodium. Because the total base, as noted above, varies but little, a change in chloride must ordinarily be compensated for by an inverse change in bicarbonate, and vice versa. Thus, when chloride is low, bicarbonate is usually high. The outstanding exception to this statement is the case in which extraneous acids are present, for example, in diabetic coma. Similarly, after prolonged hyperventilation the low carbon dioxide content of the blood may be accompanied by low sodium and almost certainly by high chloride.

Normal values usually range from 100 to 110 milliequiv. per liter of plasma.

Low values, that is, 98 milliequiv. per liter — the urinary threshold — may be encountered in a salt-free diet, and the urine may be devoid of chloride. Starvation may occasionally reduce the value to 91 milliequiv., as may the sweating leading to heat cramps. After a meal the alkaline tide due to gastric acid secretion may be accompanied by a fall in plasma chloride of 3 milliequiv. On a larger scale, as in pyloric obstruction with repeated vomiting, loss of gastric hydrochloric acid may reduce the serum chloride to less than half its normal value. Indeed, tetany may result, accompanied by a high value for plasma bicarbonate. This obviously cannot occur with achlorhydria because then the vomitus contains approximately equal amounts of sodium and chloride. In diabetic ketosis, despite the accompanying dehydration, the values may fall to 86 or 96 milliequiv. as the combined result of vomiting, diuresis, accumulation of oxybutyrate and acidosis. Although edema tends to be aggravated by administration of bicarbonate and salt, the change is usually registered by an increase in intercellular fluid rather than in sodium concentration. In pneumonia there may be a drop to 80 milliequiv., for which reason some clinicians

recommend giving salt up to the point of edema. Similarly, in eclampsia a low chloride concentration is common. The results in nephritis are variable, owing to opposing trends. With edema there may be retention of salt and water in disproportionate degrees so that low, normal or high concentrations of chloride may be found. In the absence of edema, a so-called "dry" retention of chloride may occur; or there may be a chloride deficit, with or without dehydration. In terminal uremia, normal or low chlorides are usual, depending on the extent of vomiting and the effect of the loss of the renal threshold. Accordingly, for the best therapy it is necessary to know simultaneously the total base (or sodium), chloride and carbon dioxide of the serum.[33]

High values, up to 110 milliequiv. per liter, may be induced by giving 40 gm. of salt a day. In diarrhea the value is normal or slightly increased. Preceding a diuresis, whether spontaneous or due to mercurial diuretics, it may rise to 120 milliequiv. In acute or chronic glomerulonephritis or in gouty nephritis, there also may be a slight increase.

Infants show extraordinary fluctuations in various illnesses. In bronchopneumonia, values of 79 to 93 milliequiv. per liter have been reported, and in lobar pneumonia 74 to 100 milliequiv. Infantile tetany may show 78 to 100 and nutritional edema 75 to 101 milliequiv. Some of the most bizarre disturbances involving electrolyte balance occur in infants and children.[33]

Blood Carbon Dioxide

Because the corpuscles contribute significantly to the binding of carbon dioxide under physiologic circumstances, it is justifiable to use whole blood for this determination. Detailed methods are given by Peters and Van Slyke.[3] Nevertheless, in many laboratories plasma is being used. There is the additional complication that one may determine either the *content* at the time when sampled or the combining *capacity* after equilibration with a standard gas mixture like alveolar air. Furthermore, plasma gives different values depending on whether the red cells have been removed before or after equilibration — the so-called "true" or "false" plasma. It is essential, therefore, to know precisely with which combination of these possibilities one is dealing. Probably the most convenient arrangement is the gasometric determination by the Van Slyke apparatus[3] of the carbon dioxide combining capacity of the whole blood when equilibrated at 37°C. with a gas mixture containing carbon dioxide at a tension of 40 mm. of mercury and oxygen at a tension of at least 110 mm. of mercury.

Normal values range from 22 to 30 millimols per liter, or approximately 50 vol. per cent.

Low values are commonly found in infantile diarrheas, in which treatment by Hartmann's solution[34] is preferable to the administration of saline alone. Of course, any reduction in total plasma base will tend to reduce bicarbonate. In severe diabetic coma, the total carbon dioxide may fall to 3 millimols per liter, or 7 vol. per cent. Low values are also found in uremic acidosis owing to the accumulation of inorganic acids (phosphate and sulfate). In hysterical hyperpnea enough carbon dioxide may be blown off to reduce markedly the total carbon dioxide, at least temporarily.

High values occur in emphysema owing to faulty ventilation. They are occasionally found after prolonged treatment with Sippy powders for peptic ulcer. When the value reaches 40 millimols per liter, tetany usually ensues; this concentration corresponds to the absorption (without excretion) of 40 gm. of sodium bicarbonate. Of special interest are paradoxical combinations of acidosis and a high total carbon dioxide, such as may be induced by rebreathing of gas mixtures rich in carbon dioxide. One may likewise find a paradoxical alkalosis associated with a low total carbon dioxide level in the blood, such as that induced by hyperventilation. Such combinations are likely to be overlooked in routine clinical medicine. This error may be avoided by the habitual use of total base, chloride and carbon dioxide in unusual cases involving electrolyte balance.[33] The determination of carbon dioxide in the alveolar air is also helpful if conditions are favorable.

Acidity (pH)

Although the acidity of the whole blood is influenced physiologically by the red cells, it must perforce be determined in plasma. It may be measured with approximate accuracy by the careful use of an indicator, using a comparator device.[35] It is better measured electrometrically in a laboratory equipped with a glass electrode[36] or similar device, or by the use of gasometric analyses involving carbon dioxide dissociation curves.[32]

Normal values range from pH 7.35 to 7.48. Life can exist for only a short time below pH 6.9 or above 7.85.

Low values indicate acidosis, and at pH 7.0, acidotic coma sets in.

High values indicate alkalosis, and at pH 7.8, alkalotic coma occurs.

REGULATORS (VITAMINS, HORMONES, ENZYMES)

Plasma Vitamin A

The value for plasma vitamin A may be estimated approximately by photoelectric colorimetry, but the problem is still in the investigative phase and normal values are debated. The same statement may be made for plasma carotene. In carotinemia the increased color may be mistaken for

l. 224
941

icterus, but the identification is easily made because the van den Bergh determination of bilirubin will be normal. Likewise, special identification of the ether-soluble carotene is possible through appropriate tests as described by Stueck, Flaum and Ralli.[37]

Plasma Vitamin C

The value for plasma vitamin C is ordinarily determined by titrimetric[38] or colorimetric[39] analysis, involving Tillmann's oxidation-reduction indicator. The concentration in the plasma falls much sooner than that of the tissues in avitaminosis, and indeed falls rapidly in acute febrile infections. Analyses of the plasma may therefore produce false alarms because the tissues may still be moderately well supplied with vitamin when the plasma is devoid of it.

Normal values in the plasma or serum approximate 0.8 mg. per 100 cc., but wide variation in values is reported from different laboratories. Thus the plasma often contains 1.3 to 2.8 mg. and the red cells 0.8 to 1.7 mg. In persons without clinical scurvy the values may go at least as low as 0.1 mg. for considerable periods. In frank scurvy the value is approximately 0.

Plasma Vitamin K

Plasma vitamin K has assumed importance in cases involving the clotting of blood, as in malnutrition, jaundice and hemorrhagic diatheses. It is ordinarily determined in terms of the prothrombin clotting time. Several accurate methods are available, as discussed previously in the *Journal*,[2] but the so-called "bedside test" of Smith, Ziffren, Owen and Hoffman[40] serves for routine work. Normal values depend on the procedure involved.

Low values occur most frequently in jaundice, because the presence of bile is essential to the absorption of vitamin K by the intestine. Nevertheless, low values (prolonged prothrombin clotting time) may be encountered in other conditions. Among these are the chronic diarrheas, similar to those encountered in sprue, regional ileitis, hemorrhagic disease of the newborn and various diseases of the liver. The test is of great help, not only in diagnosis and in prophylaxis of hemorrhage, but also in following the effectiveness of therapy. In liver necrosis, the administration of vitamin K may fail to restore the plasma prothrombin level to normal.

Plasma Phosphatase

Alkaline phosphatase. The determination of this enzyme in plasma depends on the amount of organic phosphate converted into inorganic phosphate in a given time under standard conditions[41, 42] Usually incubation for an hour or longer is required. The values in the literature are confused because various laboratories have used different procedures and different units. Fortunately, the new Bodansky unit is close to the new Jenner–Kay unit.

Normal values range from 1.5 to 4 units, possibly 7. There is much clinical variation, but typical values follow: hyperparathyroidism 25 units; active localized Paget's disease, 5 to 20 units; active diffuse Paget's disease, 50 to 135 units; active rickets at four months to two years of age, 30 to 165 units. Although alkaline phosphatase is ordinarily employed in conditions involving bone disease, confusion may arise because high values are found in many cases of jaundice.[43] Thus with jaundice showing an icteric index above 15 one might possibly find an alkaline phosphatase of 40 units, but the values vary greatly.

Acid Phosphatase. Ordinarily there is only a little acid phosphatase in the plasma. This term means an enzyme that operates optimally in acid solution. Such an enzyme occurs in the prostate gland, however, and Gutman[44] has shown that in cancer of the prostate a high concentration of this enzyme may appear in the plasma. Such a finding obviously may be of high diagnostic value.

Serum Amylase

Serum amylase, an enzyme that accelerates the hydrolysis of starch or glycogen, has been determined by several methods. A convenient one is that used by Cole.[45] Each investigator employs his own system of units, so that standard values cannot be given. The most useful clinical finding is the extremely high serum amylase activity found almost invariably in acute pancreatitis. In the diagnosis of acute surgical conditions of the abdomen, this test may be of great value.

Plasma "Hormonal" Iodine

If care is taken to eliminate extraneous iodide, the organically bound iodine of the plasma offers a convenient method of studying thyroid disease.[2] Reliable practical methods are described by Salter.[40]

Normal values range from 4 to 8 microgm. per 100 cc. (A microgram is one millionth of a gram.)

Low values, that is, from 0.5 to 3.5 microgm. per 100 cc., are encountered in myxedema and cretinism, and in polyglandular syndromes, like Simmonds's cachexia, that involve thyroid failure.

High values are found in hyperthyroidism (Graves's disease), in toxic nodular goiter and in some cases of acromegaly. Such values range from 8 to 18 microgm. per 100 cc. and possibly higher, depending on the degree of thyrotoxicosis. Long-standing cases of so-called "hyperthyroidism," however, may show normal iodine values, presumably

because the thyroidal stores of iodine have been exhausted.

Technical Details

The laboratory technician is frequently vexed by the careless preliminary handling of blood samples. The following are typical examples of mishandling that should be avoided: The container is dirty, or the stopper leaks. The blood is clotted. A huge excess of anticoagulant has been used, thus interfering with subsequent analytical procedures. The carbon dioxide content of a blood sample is requested, when inadequate — or no — precautions have been taken to avoid loss of carbon dioxide into the atmosphere. Calcium determination is requested in plasma treated with oxalate, which, of course, removes the calcium. Sodium oxalate is used as anticoagulant when analysis for sodium or for total base is requested. The blood is stale or hemolyzed when received at the laboratory. The patient had not been fasting when the blood was drawn.

* * *

In the foregoing synopsis it has been pointed out that clinical chemistry is merely the essence of physiological investigations in pathologic states. It has been emphasized that so-called "normal" values vary according to the procedure used in the laboratory in which they are determined. Therefore it is essential to discover the normal range under individual circumstances. It has also been pointed out that determinations in serum or plasma are usually preferable to determinations in whole blood, which is a mixture of cells and surrounding fluid. Proper interpretation of these values requires keen insight into physiologic mechanisms at work in disease, and such interpretation must be tempered constantly with common sense. The routine laboratory tests are subject to various fundamental as well as incidental errors, and consequently such data should not take precedence over clean-cut bedside observations. Laboratory data merely supplement careful clinical study of the patient in toto.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27011

PRESENTATION OF CASE

A twenty-four-year-old woman entered the hospital complaining of abdominal pain, nausea and vomiting of approximately nine days' duration.

The patient was first admitted to this hospital seven years before her present illness with a history of chronic cough and sputum aggravated by frequent upper respiratory infections. The cough gradually became more severe, the sputum more copious and occasionally associated with hemoptysis. Physical and x-ray examinations confirmed the diagnosis of bronchiectasis in the left lower lobe. The left phrenic nerve was crushed, but there was no alleviation of symptoms, so that fourteen months later the first stage of a lobectomy was performed. Six months later the lobe was removed and an uneventful convalescence followed. The patient remained well and active for the next five years; she married and bore one child. Following her pregnancy she had bilateral breast abscesses.

Three weeks before admission she returned to the Out Patient Department with the following story. Two months previously she started to suffer from migratory pains in the ankles, knees, wrists, fingers, elbows, shoulders and back and the first three of these became red, swollen and tender. The tips of the fingers were blanched and sore. In addition she felt weak and tired, and noticed some palpitation and shortness of breath. She stated that the lymph nodes in her neck were swollen occasionally and that she had lost 12 pounds in weight. For the two weeks prior to admission she had frequency of urination, with nocturia once a night. On examination the patient walked with difficulty because of the pain in her joints. The gums were tender and bleeding, and the anterior cervical lymph nodes tender. The thyroid gland was somewhat enlarged. The middle fingers of both hands were spindle shaped; both ankles and the left knee and wrist were swollen, warm and tender, without limitation of movement. The heart was not enlarged, but there was a loud systolic murmur heard best at the pulmonic area; the blood pressure was 110 systolic, 70 diastolic. The pulmonic second sound was greater than the aortic second. The temperature was 99.4°F., the pulse 98. Examination of the urine showed a + test for albumin with 4 red and 12 white blood cells per high-power field. The patient was ordered to bed for one month on a high-calorie, high-vitamin diet, but returned nine days later. It appeared that after she had been seen in the Out Patient Department she noticed in her left flank a dull ache that soon shifted to the left upper quadrant and became very severe. This pain kept her awake, was not relieved by position and was accompanied by nausea, vomiting and constipation. She felt feverish and had one chill. She took a laxative and felt much better after a bowel movement. In addition there were burning, frequency and urgency on urination. Although the pain persisted as a dull ache, it did not return in all its severity until the morning of admission, when it was again accompanied by nausea and vomiting. The joint symptoms had improved remarkably and at the time of admission had disappeared completely. She had lost 19 pounds in the previous two months.

The patient had had her tonsils and adenoids removed fourteen years previously. The family history was irrelevant.

On examination the patient was well developed and well nourished, but pale, and she appeared chronically ill. She was very restless and complained of pain in the left flank. The head, eyes, ears, nose and throat were normal. Lobectomy scars were present in the left chest posteriorly and laterally. The heart was not enlarged to percussion and the rhythm was normal, but there was a loud systolic murmur over the pulmonic area and a faint systolic murmur at the apex. The pulmonic second sound was greater than the aortic second; the blood pressure was 110 systolic, 70 diastolic. The left diaphragm was high, the lungs were clear, and there was no shift of the mediastinum. The abdomen was soft, but an area of tenderness was present high in the left flank near the costovertebral angle, with moderate muscle spasm in this area. Pelvic and rectal examinations were negative except for a moderate cystocele. The reflexes were active and equal, and all joints appeared normal.

The temperature was 100°F., the pulse 90, and the respirations 20.

Examination of the urine showed a ++++ test for albumin with 5 to many white blood cells and 10 to 30 red blood cells per high-power field. The specific gravity varied from 1.002 to 1.012. Several cultures grew variously colon bacilli, *Staphylococcus aureus, Staph. albus* and diphtheroids. Examination of the blood showed a red-cell count of

3,250,000 with a hemoglobin of 55 per cent, and a white-cell count of 14,000 of which 81 per cent were polymorphonuclears, 17 per cent lymphocytes and 2 per cent monocytes, with no eosinophils or basophils. The nonprotein nitrogen of the blood serum was 55 mg. per 100 cc., and a blood culture and a blood Hinton test were negative. The serum protein was 5.8 gm., the phosphorus 7.1 mg., and the calcium 8.7 mg. per 100 cc.; the blood chlorides were 89.8 milliequiv. per liter, and the carbon dioxide combining power was 19.8 milliequiv. per liter. A phenolsulfonephthalein test showed no excretion of the dye in fifteen minutes, and less than 5 per cent in thirty minutes. An intravenous pyelogram showed a large quantity of gas in the small and large bowels, without definitely dilated loops. The kidney outlines were indistinct but sharp where visible; both were grossly enlarged but showed no lobulation. The intravenous dye was excreted poorly. The left kidney pelvis was not definitely visualized; the right pelvis was moderately enlarged, and the calyxes appeared distorted, but normal in size. A bilateral retrograde pyelogram showed slight dilatation of the left kidney pelvis and calyxes. The right kidney calyxes showed multiple irregular deformities. A chest plate showed the old resection of the left seventh and eighth ribs and a high diaphragm on the left side. The left costophrenic angle was obliterated.

A cystoscopic examination showed a normal bladder and normal ureteral orifices. The catheters passed easily into the kidneys, and a normal drip of clear urine was obtained on the right, but none on the left. On the tenth hospital day the patient started to hiccough and vomited a gray fluid, which was guaiac positive. The nonprotein nitrogen had risen to 110 mg. per 100 cc. Four days later catamenia began two weeks early, but the flow ceased within two days. Sixteen days after admission, the patient complained of a "white sheet" in front of her eyes and singing in the ears. Ophthalmoscopic examination was negative, and she was able to count fingers. A few minutes later she became comatose and rigid, with stertorous breathing, and blood-flecked saliva oozed from her mouth. Consciousness quickly returned with little subjective change, and though she complained of weakness in the lower extremities physical examination was negative except for a questionable temporal-field defect on the left; the blood pressure was 140 systolic, 90 diastolic. The patient appeared to improve for a day, but then became drowsy, and purpuric spots were noticed about the elbows. The next day she had a hemoptysis and complained of a sharp chest pain; bronchial rales were heard over the entire right chest. By the following day she was semicomatose, with rapid respirations and slight cyanosis. The pulse rate was 110, and the blood pressure 140 systolic, 90 diastolic; rales were present at both lung bases. The nonprotein nitrogen was 87 mg. per 100 cc., with a carbon dioxide combining power of 16.9 milliequiv. per liter. In the evening she suddenly coughed up 100 cc. of pure blood, and died two and a half hours later, three weeks after admission.

Differential Diagnosis

Dr. Walter Bauer: I had thought that we members of the arthritic group saw all the patients who came into the medical wards with arthritis. However, this is one we did not see. Since reading the report, I wish we had.

I doubt if the events chronicled in the first paragraph of this patient's history have anything to do with the present illness.

As I see it, my problem is a twofold one: first, to establish if possible the nature of the lesion responsible for the renal failure, and secondly, to determine whether the antecedent arthritis was or was not related to the renal disease. In other words, should I attempt to explain the entire clinical picture on the basis of one disease or should I make several diagnoses? In a young adult, it is usually safer to make one diagnosis. In adults above fifty, it is much more hazardous.

I first thought this patient suffered from pyelonephritis with obstruction of the left ureter, but the subsequent findings do not bear out this diagnosis. The absence of chills and the scanty evidence of fever would be most unusual, and we do not associate any type of arthritis with pyelonephritis.

Bilateral polycystic disease of the kidneys with an associated secondary gouty arthritis would be considered by some. I should hesitate to make such a diagnosis, because I have never been willing to believe that there is such a disease as secondary gouty arthritis, and because the x-ray findings are not like those of polycystic disease of the kidneys.

Could this patient have had nephritis? I should say that she could. The enlarged kidneys would rule out a diagnosis of chronic glomerular nephritis, with secondary hyperplasia of the parathyroid glands and renal osteitis fibrosa cystica. However, enlarged kidneys are seen in acute and subacute glomerular nephritis.

There are many reasons why I should prefer to stick to this diagnosis. It would help explain many other features of this patient's disease. I

believe that she suffered from recurrent attacks of pulmonary edema, a not uncommon finding in acute nephritis. The pulmonary changes occurring under such conditions can be responsible for confusing and bizarre x-ray findings. They may vary greatly from day to day. This type of pulmonary edema is probably another manifestation of the diffuse capillary damage that can take place in acute nephritis.

Can we possibly connect the arthritis with the nephritis? Coburn* has described nephritis as a complication of rheumatic fever. It is usually very mild, and the diagnosis rests largely on the urinary findings. I doubt if it ever progresses to a stage where renal failure would be evident. There are no findings in this record to suggest that the patient was suffering from periarteritis nodosa, nor are the renal findings consistent with this diagnosis. If she had rheumatoid arthritis and nephritis, I should not consider them causally related. The joint involvement was symmetrical, a characteristic finding of rheumatoid arthritis but a rare finding in the other arthritides. However, one very rarely sees red, hot joints in rheumatoid arthritis.

I shall try to rebuild the clinical picture in the following manner: first, a hemolytic streptococcal infection (not recorded in the clinical record); secondly, a specific infectious arthritis resulting therefrom; and finally, the development of an acute glomerular nephritis with complicating pulmonary edema. The sudden exitus may have been due to a cerebral hemorrhage or a pulmonary infarct.

Dr. Aubrey O. Hampton: The right kidney is much more clearly outlined than the left and is certainly enlarged. After the intravenous dye we see the right kidney pelvis faintly, whereas the left is not visible. In the retrograde pyelograms there are deformities of the right pelvis, but these correspond more closely to the picture of a hypertrophied kidney than to that of a polycystic one. It must be admitted that after a unilateral nephrectomy the pyelogram of the remaining kidney, which undergoes considerable compensatory hypertrophy, may become difficult to distinguish from that of a polycystic kidney. In this case, however, polycystic disease is ruled out by the absence of deformity of the left pelvis. The left ureter is well demonstrated and is normal. The lungs are normal except for a shadow that I interpret as the stump of the resected lower lobe. The diaphragm is high, probably because of the resected lobe. The heart is normal.

*Coburn, A. F. *The Factor of Infection in the Rheumatic State.* 228 pp. Baltimore: Williams & Wilkins Co., 1931. P. 34.

Clinical Diagnoses

Pyelonephritis with uremia.
Pulmonary infarct?
Pulmonary edema?

Dr. Bauer's Diagnoses

Acute specific infectious arthritis (probably due to a hemolytic streptococcal infection).
Late acute or early subacute glomerular nephritis.
Pulmonary edema.
Cerebral hemorrhage?
Pulmonary infarct?

Anatomical Diagnoses

Subacute glomerulonephritis.
Cerebral hemorrhage, right occipital lobe.
Periarteritis nodosa.
Hemorrhagic pulmonary edema.
Bronchiectasis, right lower lobe.
Operative scars: lobectomy, left lower lobe; phrenectomy, left.

Pathological Discussion

Dr. Tracy B. Mallory: At the post-mortem examination we found a pair of very large kidneys, weighing 450 gm., with capsules that stripped with difficulty and left slightly granular surfaces, in other words a subacute nephritis. On microscopic examination all the glomeruli were found to be involved in the typical manner of diffuse glomerulonephritis. There was no evidence of pyelonephritis or of any obstruction in the urinary tract. I cannot explain why the intravenous dye was excreted only by the right kidney. The precipitating factor in death was a cerebral hemorrhage, and that report of questionable visual defect on the left was probably quite correct, because the patient had a large hemorrhage in the right occipital lobe. There was pulmonary edema. There was also some evidence of chronic infection in the base of the right lung, a mild degree of bronchiectasis similar to what had led to operation on the other side. When the microscopic sections came through, we were surprised to find something else. This was most obvious in the spleen, where the arteriole in each Malpighian corpuscle showed a periarterial granulomatous process. Further search quickly revealed numerous arterioles in the pancreas and in the systemic musculature, with lesions typical of periarteritis nodosa.

There certainly was nothing in the clinical history or physical findings remotely pointing toward such a diagnosis. Dr. Bauer raised the question of

rheumatic fever. The valves were quite negative, and we could find no Aschoff bodies in the myocardium; consequently, we have no positive evidence of it. On the other hand, periarteritis nodosa is seen in association with rheumatic fever with significant frequency, so that one might argue that the periarteritis was evidence of rheumatic infection. I do not know how that can be disproved.

DR. BAUER: Do you think there is any possibility of explaining everything on the basis of acute nephritis following a hemolytic streptococcal infection, which had caused the antecedent infectious arthritis? That would explain everything that occurred in this patient.

DR. MALLORY: That explanation is certainly adequate for everything except the arterial lesions. They bring up the old problem. Is periarteritis nodosa a specific disease with a single though unknown etiology, or is it possible that such lesions can develop in the course of a variety of different pathologic entities? Reliable evidence that they occur in any disease of known etiology is lacking, so that I am still slightly predisposed in favor of the first hypothesis.

CASE 27012

PRESENTATION OF CASE

A forty-nine-year-old Swedish machinist entered the hospital complaining of increasing shortness of breath and substernal pain of two years' duration.

At nine years of age, the patient spent one week in a hospital because of swelling of his feet, but could recall no other features of this illness. At fourteen he fell into the water during the winter, and for the next two weeks his feet and ankles were swollen. Each spring thereafter the swelling recurred and lasted for about a week. The patient immigrated to the United States at the age of twenty-two, and at this time noticed slight palpitation, but was able to do manual labor without distress. At twenty-seven he spent eight weeks in bed with the "flu." Two years before entry he first noticed the onset of shortness of breath and substernal pain with palpitation. In the last four months the attacks were frequent and often lasted for several minutes. The patient continued to work steadily in a shoe factory until eight weeks before entry, when his physician told him to "take it easy." He worked spasmodically until the time of admission, when an increase in the above symptoms, in addition to insomnia and anorexia, forced him to give up. He stated that he had had frequent nosebleeds for the two or three years prior to entry.

The family history was irrelevant.

On examination the patient was a well-developed, slightly jaundiced man who was dyspneic and appeared chronically ill. The neck veins were distended. Examination of the heart revealed marked enlargement to the left and a rapid, completely irregular impulse. There was a systolic murmur at the apex, and diastolic and systolic murmurs at the left sternal border. The blood pressure was 120 systolic, 80 diastolic. The lungs were clear. The liver was slightly tender and palpable four fingerbreadths below the right costal margin. There was no edema of the extremities.

The temperature was normal, the pulse 70, and the respirations 28.

Examination of the urine showed a +++ test for albumin, with frequent hyaline and granular casts. The blood showed a red-cell count of 4,470,000 with a hemoglobin of 14.5 gm. (photoelectric-cell technic), and a white-cell count of 15,600 with 70 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 59 mg., and the van den Bergh 4.7 mg. per 100 cc. A blood Hinton test was negative.

X-ray examination of the chest showed a grossly enlarged heart, the enlargement affecting all chambers. The hilar shadows were prominent, and there was hazy density extending out into both mid-lung fields. At a subsequent examination there was diffuse dilatation of the pulmonary vessels without fluid in the pleural cavities. The auricles were grossly dilated, and the apex of the heart was thick and blunt. The aorta was relatively prominent. No areas of calcification were seen in the region of the valves or the pericardium. The electrocardiogram showed auricular fibrillation; there was slight to moderate left-axis deviation, and the QRS interval in leads 1 and 3 measured from 5 to 6 mm.

Following digitalization the ventricular rate was slowed, the heart decreased in size and the nonprotein nitrogen of the blood serum dropped to 25 mg. per 100 cc. At times the patient was restless and nervous, apparently because of dyspnea. A decrease in fluid output led to the use of Salyrgan, with satisfactory diuresis. A phenolsulfonephthalein test at this time gave a 20 per cent excretion in fifteen minutes, 50 per cent in thirty minutes. The patient gradually improved and one month after admission was allowed to sit in a chair and walk about the ward. Although this activity was performed without distress, he became dyspneic with any increase in exercise. Six weeks after admission he began to go downhill, gradually became confused and disorientated, and developed Cheyne-Stokes breathing and sacral edema, with an increased pulse rate. The tem-

perature rose abruptly to 101°F. and then to 104 with a white-cell count of 13,700, but the lungs were still clear. One week later the patient became semicomatose, and he died the next day, seven weeks after admission.

Differential Diagnosis

Dr. Paul D. White: We should like to know more, particularly in regard to the details of the shortness of breath and of the substernal pain. We should also like to know whether that substernal pain was related to effort or came on in paroxysms when the patient was in bed. It seems to have been a rather indefinite pain, which might or might not have been angina pectoris.

A forty-nine-year-old man may have substernal pain and dyspnea due to either coronary disease or syphilitic aortitis. These are the two types of heart disease that come to mind first. Of course, too, he might have had a condition that had been present since early life. The swelling of the feet at the ages of nine and fourteen may have been due to a variety of things, but we naturally think of rheumatic fever. "Each spring thereafter the swelling recurred and lasted for about a week." Spring is the time, of course, when we might expect recurrence of a rheumatic infection. We should like to know if there was any statement about pain, as well as swelling of the feet.

Dr. Benjamin Castleman: There was none.

Dr. White: Generally joint pain is more pronounced than swelling in acute rheumatic infection, but sometimes there is surprisingly little of either. Finally, there is a suggestion of active rheumatic fever in the story of repeated nosebleeds, but we cannot consider it a reliable indication. Rheumatic fever is not rare in Sweden, and rheumatic heart disease is frequently found throughout northern Europe.

"At twenty-seven he spent eight weeks in bed with the 'flu'." That was twenty-two years before admission, and would bring it about the time of the great influenza epidemic. He probably had "flu" and pneumonia with it.

We may guess that the patient had had recurrent attacks of rheumatic fever, but up to the time of his immigration to this country he had had no symptoms of heart disease other than palpitation, too minor a symptom to be of importance. Since entering this country he had been quite active in manual labor. He was either a casual or a stoical Swede, I should say, certainly not neurotic, and probably rather neglectful of his health, since he continued to work despite his symptoms during the last two years.

I should like to know why he had insomnia, also if the anorexia occurred when he began to be congested and to have dyspnea. Insomnia is sometimes due to dyspnea or orthopnea. I have seen patients benefited more by digitalis than by hypnotics.

Auricular fibrillation is evident. Its onset may have been the precipitating cause of his increase of symptoms during the past two years. It is a point against syphilis, and also against coronary disease at this time.

The systolic murmur at the apex is not very important, except that it means that there is something wrong. Even if it is loud, such a murmur may be the result of functional mitral regurgitation without any intrinsic heart disease. The diastolic and systolic murmurs at the left sternal border are another thing. What they mean we cannot be sure — probably aortic regurgitation. Most patients who have aortic regurgitation with a diastolic murmur along the left sternal border have also a systolic murmur.

The blood-pressure measurement is evidence against a diagnosis of free aortic regurgitation. There is no increase in pulse pressure, so that we may assume that the aortic regurgitation causing this murmur was slight or that the murmur was due to pulmonic regurgitation. Pulmonic regurgitation may occur secondary to mitral stenosis, but we should find evidence of marked stenosis before that happens, and no such evidence is present.

"Examination of the urine showed a +++ test for albumin, with frequent hyaline and granular casts." That is not a diagnostic finding; it may be merely a part of the congestion.

"The nonprotein nitrogen of the blood serum was 59 mg., and the van den Bergh 4.7 mg. per 100 cc." They are elevated, but neither one of itself is diagnostic evidence of kidney or liver disease.

"A blood Hinton test was negative." That is a very important point, because with a man of this age aortic regurgitation brings to mind syphilitic aortitis. The chances are nine to one that there is no aortitis in the presence of a negative Hinton test.

There was an increase in the shadow of the pulmonary vessels during life, which is not shown in the post-mortem film. That may be due to failure of the left ventricle rather than to pulmonary disease or mitral stenosis.

The patient had quite a good recovery, but slow. It was a month before he was allowed to sit up.

"Six weeks after admission he began to go downhill, gradually became confused and disorientated, and developed Cheyne-Stokes breathing and sacral edema, with an increased pulse rate." Why this

disappointing development? He was getting on all right, and for no obvious reason he began to do poorly, with increasing pulse rate and cardiac failure, despite good therapy. Something new had happened. Was it infection, or possibly infarction? If it was infection, might it be recurrent rheumatic infection? There is no indication of subacute bacterial endocarditis, which is rare in the presence of auricular fibrillation. There may be rheumatic endocarditis or infarction of lungs without physical signs. There may even be myocardial infarction without symptoms or signs.

To sum up, let us take the known findings first. The patient had a big heart, auricular fibrillation and total heart failure. Those are the three things that are quite clear. He probably had aortic regurgitation. Once in a while there may be aortic regurgitation due to syphilitic aortitis, without valve deformity. A dilatation of the aortic ring may account for insufficiency of the valve, which will not be found at autopsy. We may know it is there clinically, but we do not put down organic aortic regurgitation as an essential finding at autopsy. Mitral regurgitation, with or without mitral valve disease, was present. We know that the patient had a big heart, and he might have had mitral regurgitation secondarily, but whether or not he had valve disease we cannot tell. With failure, a big heart may have mitral stenosis (or aortic stenosis) of a considerable degree without the characteristic murmurs. Finally, he may have had terminal pulmonary infection or infarction. In favor of infarction is the jaundice and the elevated serum van den Bergh.

Now comes the difficult problem, namely, the question of etiology. The best bet in view of the childhood history, the aortic regurgitation and the auricular fibrillation is rheumatic heart disease, acute and chronic. Coronary disease is less likely, and if present is superimposed. We do not see auricular fibrillation so frequently from coronary insufficiency, and we expect death more suddenly. Syphilitic aortitis is possible but not probable; it may be a complication. We have had patients with rheumatic heart disease and syphilitic aortitis combined, but I do not believe that diagnosis is more than a possibility here. Syphilitic aortitis and subacute bacterial endocarditis must be considered as unlikely possibilities. I should say that there was a complicating infection or infarct, with pulmonary infarction as a first guess.

Dr. Howard B. Sprague: I am glad to have Dr. White go through the same course of thought that I did on seeing this patient. He came to the Out Patient Department and was admitted on the service. One of the admission diagnoses was coronary disease. He had rapid auricular fibrillation, and it was very difficult to make out anything in the examination of the heart. A house officer noted a systolic murmur. When I examined the patient a little later I made the following note in the history:

> The history suggests repeated rheumatic infection of the ankles and feet in childhood. His recent progressive dyspnea and palpitation may have been brought on by auricular fibrillation, which he now shows. He has a big, forceful heart with a systolic murmur at the apex and a systolic and diastolic at the left sternal border. I believe he has a rheumatic heart with mitral regurgitation, and possibly some stenosis, and aortic regurgitation, with again a question of stenosis. The fever suggests active carditis, pulmonary embolism or phlebitis.

He was digitalized, given mercurials, and during the next three or four days the murmurs became obvious on examination. There was a note of a systolic murmur at the aortic area, without any thrill. He then, as has been recounted, failed to make satisfactory progress, and again we asked if this were active rheumatic infection in the heart or in the lung or multiple small pulmonary infarcts, or thrombosis elsewhere in the body that we could not discover.

Dr. White: Did the aortic systolic murmur become more distinct when he improved?

Dr. Sprague: Yes.

Dr. White: It raises the question of aortic stenosis, of course. It may be very difficult to detect aortic stenosis in the presence of congestive failure because of the decrease of blood flow. I should like to add the diagnosis of aortic stenosis as a possibility here.

Clinical Diagnoses

Rheumatic heart disease, with combined aortic and mitral valvular lesions.
Acute bacterial endocarditis?
Cavernous sinus thrombosis?
Cerebral emboli?

Dr. White's Diagnoses

Rheumatic heart disease, with aortic regurgitation, ? aortic stenosis and relative mitral regurgitation.
Hypertrophy of the heart.
Auricular fibrillation.
Pulmonary embolism or infarction.
Chronic passive congestion.

Anatomical Diagnoses

Aortic stenosis, calcareous.
Septicemia (hemolytic streptococcus).
Cerebral and cerebellar degeneration.
Cardiac hypertrophy.

Mural thrombus, right auricular appendage.
Pulmonary infarction, recent.
Chronic passive congestion of lungs, liver and spleen.
Arteriosclerosis, coronary and aortic.
Icterus.

Pathological Discussion

Dr. Castleman: At autopsy this man had an unusually large heart, weighing 800 gm. There was hypertrophy and dilatation of all chambers. The mitral valve was perfectly normal in appearance, although it measured 12.5 cm. in circumference. There was no thickening of the margins or of the chordae tendineae to suggest rheumatic infection. The aortic valve showed marked stenosis of the calcareous type, with a lumen that admitted the tip of the index finger, probably 0.5 cm. in diameter. The valve itself measured 4 cm. in circumference. Almost all the deposits of calcium were on the sinus side of the cusps, and the appearance was characteristic of the Mönckeberg type of calcific aortic stenosis. There was no interadherence of the cusps at their commissures, such as is seen in typical rheumatic endocarditis. There were no other valvular lesions. The coronary arteries showed a fairly extensive arteriosclerosis, but no evidence of occlusion. Microscopically there were small foci of scarring in the myocardium, which may have accounted for his anginal pain, although we have seen cases of aortic stenosis alone without coronary disease associated with anginal pain. The lungs had several infarcts at both lower lobes, the emboli probably arising from mural thrombi in the right auricular appendage. The leg veins were not examined. The combination of congestion in the liver, which was moderately severe, and pulmonary infarction adequately explains the jaundice.

It is quite possible that the disease the patient had in childhood was not rheumatic fever but some other infection that may have involved the aortic valve.

Dr. White: You would agree that there was probably an infectious form of aortic-valve involvement before the calcification?

Dr. Castleman: Yes. Whether or not it was rheumatic, I am not sure.

Dr. Sprague: After Dr. Castleman found this, we went back over the autopsy cases of aortic stenosis to see if the presence of auricular fibrillation had often confused the diagnosis of aortic stenosis. I think that this can be said to be true. Rapid auricular fibrillation with severe failure, uncontrollable by digitalis, may obscure the characteristic features of the murmur and thrill at the aortic area, and the diminished aortic second sound may be erroneously attributed to cardiac failure alone.

Dr. White (later note): The apparent, insistent history of recurrent rheumatism in this patient favors, I think, rheumatic infection as responsible for the aortic stenosis, with superimposed calcification.

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THE NEW YEAR

NEARLY twenty centuries ago an apparently new star of great magnitude was observed in the east; whether this was a new comet or the conjunction of two or more heavenly bodies is today of relatively little importance. What is of significance is the belief that this star was the celestial sign of a new order beginning in the eastern world — an order based on the humanity of man to man under the leadership of the founder of Christianity.

The season of Christ's birth is probably not exactly known, nor is it of any great importance. It is perfectly natural, however, that it should have finally been placed, as accurately as the early astronomers were capable of determining the occasion, at the time of the new year. It is an accident that both Christmas and the New Year should have been established on dates that follow the winter solstice by several days; it is no accident that they should have been so closely linked together at that period of the year when the retreating sun pauses before commencing its northward journey, and the darkness of the world begins to give way before the promise of light.

That the physical illumination of the world should be in this way identified with the spiritual enlightenment of mankind seems peculiarly fitting, and it is altogether proper that our festival season of greatest solemnity and yet of greatest joy should be thus annually renewed.

This year, curiously enough, when some of the darkest days through which Christianity has passed are so recent in our memories, again a new star has appeared; this time in the west. We do not dare allow our hopes to leap too high, or our emotions to outride our reason, but if ever an omen for a new year should be revealed, this is the year when it would be most welcome.

VIRUS PNEUMONIA AND Q FEVER

WELCOME indeed is the news that the causative agent of a number of puzzling cases of atypical pneumonia, due to none of the common pathogenic bacteria, has finally been isolated and identified. This information comes from two different sources,[1, 2] and the reports appeared almost simultaneously.

In recent years, with the increasing interest in the etiologic aspects of pneumonia in relation to specific serotherapy and chemotherapy, many physicians in widely scattered localities have noted numerous cases of pulmonary infections of varying severity, but usually not fatal, in which the causative agent has not been determined by ordinary bacteriological methods. Furthermore, with the highly organized health services now available in many large universities and hospitals, it is not surprising that many of these cases of so-called "pneumonitis" or "atypical bronchopneumonia" are reported as occurring among university students and hospital personnel. Another important

factor in the recognition of these atypical pneumonias is the increasing use of roentgenograms of the chest in patients with acute febrile systemic diseases, even when symptoms of pulmonary involvement are minimal or absent.

The reported cases have followed a more or less characteristic clinical course. This has been described recently by several observers, each of whom has reported outbreaks in different parts of this country. One of the two most recent epidemics attacked fifteen employees in the laboratories of the National Institute of Health in Washington, one of whom died.[1] All these patients had high temperatures; profuse sweating frequently occurred, but true chills were rare. They felt ill and exhausted but did not have the breathing difficulty of patients with true pneumonia, or the severe body aches and pains of those with influenza. X-ray examination of the chest was found to be necessary to detect specific lesions in the lungs. It is stated, "A comparison of the clinical features and physical findings in these cases with various series reported from other sections of the United States in the past few years reveals suggestive similarities." Laboratory investigation revealed a rickettsia very similar to the one that causes Q fever in Australia. It was isolated from the blood of two of the recovered cases, and from the spleen of the fatal case.

Q fever was first described in Queensland in 1937.[2] A species of Rickettsia was recovered from cases of this disease and was shown to be distinct from other known rickettsiae.[4] Work on this particular disease has been in progress at the National Institute of Health since the spring of 1938; however, not one of the fifteen cases in the recent epidemic occurred in the wing of the building where the experimental work on Q fever was being conducted. Even more remote is linking of these cases to the recovery by officers of the United States Public Health Service, from ticks gathered in Montana, of a rickettsia that caused infection in man and was shown to be very closely related to that of Q fever.[5]

It is interesting that the clinical syndrome and the epidemiology of Q fever in Australia and of the pneumonitis observed in this country differ in some important respects. Pulmonary signs or symptoms have not been recognized in the former cases, although other features, particularly the type of fever and the severe headache, have been similar. It is possible, however, that pulmonary lesions passed unnoticed because the opportunities for roentgenography were much more limited than they are in America. Both the manifest and the latent Australian cases occurred almost entirely among butchers working in abattoirs, among foresters and among the members of the staffs of laboratories where work with the virus was being conducted. The bandicoot, a common rodent of the Australian bush, was shown to be susceptible and to be one of the reservoirs of infection, and one of the ticks commonly found in the vicinity was proved to be capable of serving as a vector.

The success of previous attempts to isolate a virus from cases of atypical pneumonia in this country was, at most, only suggestive.[6] Just after the publication of the studies at the National Institute of Health, however, there appeared a report of an investigation conducted by the International Health Division of the Rockefeller Foundation.[2] These workers recorded the isolation of a filterable virus from the pharyngeal washings of four patients with acute pneumonitis that was capable of producing pulmonary consolidation following intranasal inoculation in the wild mongoose. The etiologic relation of the virus to the human and the experimental disease was established by demonstrating the development of neutralizing antibodies in the course of convalescence from the infection. The mongoose — an animal similar to the ferret, which has been so helpful in the studies of influenza — is not susceptible to known strains of influenza virus. Importation of the animal into this country is prohibited, so that the investigations were carried out in Kingston, Jamaica, with infected materials obtained in New York City.

It remains to be seen whether the workers at the National Institute of Health and those of the Rockefeller Foundation are dealing with the same agent or virus. It seems likely that many living agents, related and unrelated, will ultimately be

implicated, and these studies will undoubtedly stimulate further research, as did those concerned with the discovery of the viruses of influenza. One may now look forward to the rapid unfolding of many interesting aspects in regard to virus pneumonias.

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MEDICAL EPONYM

Fowler's Position

In an article entitled "Results in Diffuse Septic Peritonitis Treated by the Elevated Head and Trunk Position" in *Medical News* (**84**:1011, 1904), Russell S. Fowler (1848–1906), surgeon to the German Hospital, Brooklyn, New York, describes this position as follows:

> Directly after operation the patient is placed in the elevated head and trunk position. This may be done by placing a chair or stool beneath the head-piece of the bed. At the German Hospital, we employ a frame consisting of two side supports and a central bar connecting the two. . . . This frame is secure and allows of different levels being employed. The elevation should never be less than one foot. A folded pillow is placed against the buttocks and through the fold of the pillow is passed a stout bandage which is tied on each side to the head of the bed. This allows the patient to rest comfortably, and maintains his position without exertion on his part.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

Pregnancy in a Patient with Pre-Existing, Complete Heart Block

Mrs. L. B., a twenty-eight-year-old primipara, was first seen in the hospital on August 28, 1928, when approximately two months pregnant, because of threatened miscarriage.

The family history was unknown. The patient's early medical history was noncontributory. It had been known that the patient since the age of twelve years had had a very slow pulse. She had no symptoms referable to the heart, however, until the age of nineteen, when she suddenly fainted while playing field hockey and later was told that she had almost died. In 1925 an electrocardiogram showed complete auriculoventricular dissociation, and a diagnosis of complete heart block was made. Comparatively speaking, the patient was free from any cardiac symptoms. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted three to four days with no discomfort. The last normal period began on June 20, making the expected date of confinement March 27, 1929.

About ten days before she was seen in the hospital the patient had a little bloody discharge. This was followed by a slight amount of staining. Physical examination showed a tall, rather thin woman who looked the picture of health. The physical examination was negative, except for the heart, which was slightly enlarged. The apex was seen and felt in the fifth intercostal space 9.5 cm. from the midsternal line, and the left border of dullness corresponded to the same area. The right border was 3 cm. from the midsternal line, and the supracardiac dullness was 5.5 cm. in width. The cardiac rate was 44 per minute, with slight sinus arrhythmia. The heart sounds were of good quality. The auricular sounds were not discernible. There was a harsh, loud, rather musical systolic murmur heard best at the apex but present all over the precordium. The blood pressure was 110 systolic, 70 diastolic. Vaginal examination showed the cervix in the normal axis, the fundus retroverted.

Once a month during the following weeks of pregnancy the patient returned to the hospital for twenty-four hours. She was examined and weighed. A twenty-four-hour urine analysis was made, and an electrocardiogram and a seven-foot plate of the heart with fluoroscopic examination were obtained at each visit. At no time were there any serious symptoms referable to the heart. The patient gained weight slowly; the blood pressure remained between 120 and 130 systolic, 70 and 80 diastolic. There was a slight increase in the rate of both the ventricles and auricles. Toward the end of December she became somewhat overtired, and complained of palpitation and a sense of constriction in the precordium toward the end of the day. She was advised to rest more, and at her next visit all the cardiac symptoms had disappeared; they did not recur.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

On March 20, 1929, the patient was admitted to the hospital to stay at rest until she went into labor. Examination during this period showed the cervix to be entirely obliterated and very soft; the head was well engaged. She was therefore allowed to go into normal labor, which she did after spontaneous rupture of the membranes at noon on March 31. At 3:00 p.m. she was having unsatisfactory pains and was given subcutaneously 2 minims of Infundin. Labor started satisfactorily and continued until 4:30 p.m., when the pains let up somewhat, and she was again given 2 minims of Infundin. Inhalation of nitrous oxide was started as an analgesic at this time. At 5:30 p.m. the head was in sight, and under ether anesthesia a low-forceps delivery was done.

The child was normal in every way and cried immediately. During labor the patient's pulse reached a maximum rate of 76 and was of good quality; the patient was warm and pink. The cardiac rate dropped to 60 immediately after delivery and to 44 at the time of discharge from the hospital, three weeks after the baby was born.

Examination of the heart one year and eight months after delivery showed the auricular and ventricular rates to be the same as before pregnancy; the size of the heart by x-ray films and by percussion was essentially the same. The heart sounds were of good quality; the loud systolic murmur was still present but had not changed in intensity or type.

Comment. This case was reported in the November, 1931, issue of the *American Journal of Obstetrics and Gynecology*. It is referred to again because of its rarity and in an attempt to show that heart block in itself is a contraindication neither to pregnancy nor to pelvic delivery.

POSTGRADUATE EXTENSION COURSES

The postgraduate extension courses are sponsored by the Massachusetts Medical Society in cooperation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau. Registration is free to all legally registered physicians of the Commonwealth. For further information the district chairman of postgraduate instruction should be consulted.

The programs for the winter sessions are as follows:

Middlesex East District: Melrose

SUBJECT	DATE
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	January 7
The Clinical Recognition of the Types of Jaundice and Recent Advances in Their Treatment	January 14
Chemotherapy in the Treatment of Gonococcal Infection	January 21
Pediatric Case Discussions	January 28
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	February 4
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	February 11
Obstetric Infections: Diagnosis and treatment	February 18
Head Colds and Complications	February 25

Meetings to be held at the Melrose Hospital, Tuesdays, at 4:15 p.m.

Walter H. Flanders, M.D., *Chairman*
28 Rowe Street, Melrose

Middlesex South District: Cambridge

SUBJECT	DATE
Management of Abdominal Distention	January 7
Pediatric Case Discussions	January 14
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	January 21
Diet and Vitamins in Surgery	January 28
Obstetric Complications with Case Histories and Clinical Problems	February 4
Chemotherapy in the Treatment of Gonococcal Infection	February 11
Acute Abdominal Pain: Its interpretation and management	February 18
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	February 25

Meetings to be held at the Cambridge Hospital, Mt. Auburn Street, Tuesdays, at 4:00 p.m.

Dudley Merrill, M.D., *Chairman*
51 Brattle Street, Cambridge

Norfolk District: Norwood

SUBJECT	DATE
Obstetric Complications with Case Histories and Clinical Problems	January 9
Dermatitis and Eczema (see below for questions to be discussed)	January 16
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	January 23
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	January 30
Acute Abdominal Pain: Its interpretation and management	February 6
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	February 13
Chemotherapy in the Treatment of Gonococcal Infection	February 20
Pediatric Case Discussions	February 27

Meetings to be held at the Norwood Hospital, Thursdays, at 8:30 p.m.

Hugo B. C. Riemer, M.D., *Chairman*
Norwood. Office: 128 Newbury Street, Boston

Norfolk South District: Quincy

SUBJECT	DATE
Chemotherapy in the Treatment of Gonococcal Infection	January 6
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	January 13
Obstetric Infections: Diagnosis and treatment	January 20
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	January 27
Dermatitis and Eczema (see below for questions to be discussed)	February 3
Pediatric Case Discussions	February 10
Nutritional Deficiencies and the Uses of Preparations of Vitamins	February 17
Diagnosis, Treatment and Prognosis of Central-Nervous-System Syphilis	February 24

Meetings to be held at the Quincy City Hospital, Mondays, at 8:30 p.m.

David L. Belding, M.D., *Chairman*
Hingham. Office: 80 East Concord Street, Boston

Suffolk District: Boston

SUBJECT	DATE
Head Colds and Complications	January 9
Therapeutic Uses of Preparations of Endocrine Glands: Thyroid gland, pituitary gland, ovary, testis and adrenal cortex	January 16
Pediatric Case Discussions	January 23
Chemotherapy in the Treatment of Gonococcal Infection	January 30
Dermatitis and Eczema (see below for questions to be discussed)	February 6
Acute Abdominal Pain: Its interpretation and management	February 13
Diagnosis, Treatment and Prognosis of Central-Nervous-System Syphilis	February 20
Obstetric Complications with Case Histories and Clinical Problems	February 27

Meetings to be held in John Ware Hall, Boston Medical Library, Thursdays, at 4:30 p.m.

Reginald Fitz, M.D., *Chairman*
319 Longwood Avenue, Boston

The following questions will be discussed in the course on dermatitis and eczema:

Is there such a thing as eczema?

Is allergy fact or fiction?

Are skin tests of value in dermatology?

Are fungous infections (athlete's foot) as prevalent as we are led to believe?

With the diagnosis made, what should be the treatment of common cutaneous eruptions?

Faculty for the Extension Courses

Dermatology. Chairman: Dr. John G. Downing; instructors: Drs. John Adams, Jr., Leonard E. Anderson, Bernard Appel, J. Harper Blaisdell, G. Marshall Crawford, Francis P. McCarthy, Mildred L. Ryan, Jacob H. Swartz and Maurice M. Tolman.

Ear, Nose and Throat. Chairman: Dr. LeRoy A. Schall; instructors: Drs. Charles T. Porter, Lyman G. Richards and John R. Richardson.

Gonorrhea. Chairman: Dr. Oscar F. Cox; instructors: Drs. Sylvester B. Kelley and P. N. Papas.

Medicine. Chairmen: Drs. Chester S. Keefer and Robert T. Monroe; instructors: Drs. Fuller Albright, Clifford L. Derick, E. Stanley Emery, Eugene C. Eppinger, Marshall N. Fulton, G. Philip Grabfield, Franz Ingelfinger, Charles A. Janeway, Harold J. Jeghers, William T. Salter, Charles L. Short and Maurice B. Strauss.

Obstetrics. Chairmen: Drs. Meinolf V. Kappius and Roy J. Heffernan; instructors: Drs. Christopher J. Duncan, M. Fletcher Eades, A. Gordon Gauld, Thomas R. Goethals, James C. Janney, Foster S. Kellogg, Joseph W. O'Connor, Louis E. Phaneuf, John Rock, Judson A. Smith and Raymond S. Titus.

Pediatrics. Chairmen: Drs. Warren R. Sisson and James M. Baty; instructors: Drs. Elmer W. Barron, John A. V. Davies, Louis K. Diamond, R. Cannon Eley, Joseph Garland, Harold W. Higgins, Lewis W. Hill, Edwin H. Place and Clement A. Smith.

Surgery. Chairmen: Drs. Howard M. Clute and Leland S. McKittrick; instructors: Drs. Hollis L. Albright, Arthur W. Allen, Franklin G. Balch, Jr., Marshall K. Bartlett, William E. Browne, Richard B. Cattell, Edward A. Edwards, Henry H. Faxon, Jacob Fine, E. Parker Hayden, Thomas H. Lanman, Robert R. Linton, Charles C. Lund, Champ Lyons, Henry C. Marble, E. Everett O'Neil, Neil W. Swinton and Irving J. Walker.

Syphilis. Chairman: Dr. Francis M. Thurmon; instructors: Drs. William P. Boardman, Rudolph Jacoby and C. Guy Lane.

Teaching Clinics in Gonorrhea and Syphilis

The Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health and the United States Public Health Service is again sponsoring teaching clinics in gonorrhea and syphilis. Registration in these teaching clinics is free; all expense of teaching is met by the sponsoring organizations. Clinic schedules are listed below; any legally registered physician in the Commonwealth may attend for one or more days.

Gonorrhea Clinics at the Boston Dispensary. These are open daily from 9:30 to 11:30 a.m., and on Monday, Wednesday and Friday evenings from 6:00 to 8:00. Dr. Oscar F. Cox is in charge. Write or telephone for additional information: Gonorrhea Clinic, Boston Dispensary, Boston.

Syphilis Clinics at the Massachusetts General Hospital. These are held in the Out Patient Department, South Medical Service, on Tuesday and Wednesday from 10:00 a.m. to 12:00 noon. Dr. G. Marshall Crawford is in charge. Write or telephone for additional information: South Medical Service, Massachusetts General Hospital, Boston.

POSTGRADUATE EXTENSION LIBRARY

The Massachusetts Medical Society through the cooperation of the Massachusetts Department of Public Health and the United States Public Health Service plans to provide library extension service in connection with the Society's program of postgraduate education. The funds have been provided by the United States Public Health Service; the Boston Medical Library will be charged with the operation, purchase of books and so forth; and with loaning them to physicians by mail or express.

This library service will be ready in the near future; details will be published in the *Journal*. Lists of references about each course will be available at the postgraduate extension courses. Further information may be obtained by addressing Medical Library Extension Service, 8 Fenway, Boston.

MISCELLANY

NEW TUFTS SCHOLARSHIPS

The Charles Hayden Foundation, through its president, J. Willard Hayden, has awarded a grant of $10,000 to Tufts College Medical School to be used for scholarships for selected members of the entering class in that school next fall.

Following the regular plan of the Charles Hayden Memorial Scholarships in other institutions, a portion of this total will be used for outright scholarships during the first year of medical study. The remainder will be held as a special loan fund to be used in upper-class years by those who hold Hayden scholarships during the first year.

Dr. Leonard Carmichael, president of Tufts College, in announcing the gift hailed it as a definite benefit to able and worthy young men who might otherwise be debarred from entering the medical profession. He added that the addition of these scholarships will help further the college's aim of training young men who look forward to careers as modern general practitioners. "Since the Tufts College Medical School trains more doctors for New England than any other medical school in the country," President Carmichael stated, "the gift will be welcomed by the communities throughout this section, as well as by needy and capable students."

Dr. Cadis Phipps will serve as chairman of the committee administering the scholarship grants.

NOTE

On December 16, Dr. Frank H. Lahey, of Boston, delivered the second Floyd Wilcox McRae Memorial Lecture before the Fulton County Medical Society, of Atlanta, Georgia. The title was "The Management of Gastric, Duodenal and Jejunal Lesions."

NOTICES

ANNOUNCEMENT

A. H. DELMAN, M.D., announces the removal of his office from 479 Beacon Street, to 371 Commonwealth Avenue, Boston.

HARVARD MEDICAL SOCIETY

There will be a meeting of the Harvard Medical Society on Tuesday, January 14, in the amphitheater of the Peter Bent Brigham Hospital at 8:15 p.m. Dr. A. Rosenblueth will speak on "A Physiological Analysis of Abnormal Neuromuscular Function."

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, January 21, at 12 m. Dr. George Levene will speak on "The Relation of Pituitary Function and Mental Development."

Physicians are cordially invited to attend.

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, formerly concertmaster of the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

PETER BENT BRIGHAM HOSPITAL

There will be a seminar of the medical staff of the Peter Bent Brigham Hospital on Wednesday, January 8, in the students' laboratory of the hospital at 12:15 p.m.

PROGRAM

Physiologic Changes in Artificial Fever in Relation to Thermal Exchange. Dr. John G. Gibson, 2nd.
Discussion of Problems in the Medical Clinic.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a. m.

MEDICAL CONFERENCE PROGRAM, JANUARY–FEBRUARY

Tuesday, January 7 — Public Health in National Defense. Dr. H. D. Chope.
Wednesday, January 8 — Hospital case presentation. Dr. S. J. Thannhauser.
Thursday, January 9 — The History of Pancreatic Diabetes. Dr. Martin Nothmann.
Friday, January 10 — Renal Disease and Hypertension. Dr. W. K. Leadbetter.
Saturday, January 11 — Hospital case presentation. Dr. S. J. Thannhauser.
Tuesday, January 14 — Intestinal Intubation. Dr. Louis Zetzel.
Wednesday, January 15 — Hospital case presentation. Dr. S. J. Thannhauser.
Thursday, January 16 — Chorioepithelioma. Dr. J. T. Smith.
Friday, January 17 — The Present Status of Pneumonia Therapy. Dr. Maxwell Finland.
Saturday, January 18 — Hospital case presentation. Dr. S. J. Thannhauser.
Tuesday, January 21 — Vitamin B Deficiency. Dr. Stuart Meiklejohn.
Wednesday, January 22 — Hospital case presentation. Dr. S. J. Thannhauser.

Thursday, January 23 — Fissure in Ano. Dr. E. T. Whitney.
Friday, January 24 — Pregnancy Complicating Diabetes. Dr. Priscilla White.
Saturday, January 25 — Hospital case presentation. Dr. S. J. Thannhauser.
Tuesday, January 28 — Clinic on Tumors of the Breast. Dr. W. M. Shedden.
Wednesday, January 29 — Hospital case presentation. Dr. S. J. Thannhauser.
Thursday, January 30 — Sulfathiazole in Gonococcal Infections. Dr. O. F. Cox.
Friday, January 31 — Clinicopathological conference. Drs. J. C. Aub and H. E. MacMahon.

FREE PUBLIC LECTURES

Harvard University has recently announced the subjects and speakers in its course of free public lectures on medical topics that are given each year at the Harvard Medical School. As usual these will be given in the amphitheater of Building D at 4:00 p.m. on Sundays. The schedule is as follows:

January 5. The Common Cold and How to Treat It. Dr. William B. Breed.
January 12. Hormones in Children. Dr. Joseph C. Aub.
January 19. How Accidents Happen. Dr. Henry C. Marble.
January 26. Medical Aids to Justice. Dr. Alan R. Moritz.
February 2. Modern Advances in Surgery. Dr. Oliver W. Cope.
February 9. Medical Problems Presented by Selective Service. Dr. Frederick F. Russell.
February 16. The Use and Abuse of Vitamins. Dr. Maurice B. Strauss.
February 23. Fatigue and Health. Dr. David B. Dill.
March 2. The Transfusion of Blood and Blood Banks. Dr. Carl W. Walter.
March 9. The Pathway of Medical Discovery. Dr. Reginald Fitz.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, January 5

Sunday, January 5

†4 p.m. The Common Cold and How to Treat It. Dr. William B. Breed. Free public lecture. Harvard Medical School, Building D.

†4 p.m. The Common Background of Many Symptoms. Dr. Arlie V. Bock. Public health lecture. Cambridge Hospital, Margaret Jewett Hall.

Monday, January 6

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, January 7

*9–10 a.m. Public Health in National Defense. Dr. H. D. Chope. Joseph H. Pratt Diagnostic Hospital.

12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

8:15 p.m. Some Recent Advances in the Endocrinology of the Female. Dr. Ephraim Shorr. Greater Boston Medical Society. Beth Israel Hospital, Boston.

Wednesday, January 8

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital.

12:15 p.m. Physiologic Changes in Artificial Fever in Relation to Thermal Exchange. Dr. John G. Gibson, 2nd. Peter Bent Brigham Hospital.

*2–4 p.m. Headache. Drs. E. C. Cutler and J. Romano. Peter Bent Brigham Hospital.

Thursday, January 9

*8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital.

*9–10 a.m. The History of Pancreatic Diabetes. Dr. Martin Nothmann. Joseph H. Pratt Diagnostic Hospital.

Friday, January 10

*9–10 a.m. Renal Disease and Hypertension. Dr. W. K. Leadbetter. Joseph H. Pratt Diagnostic Hospital.

Saturday, January 11

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.
†Open to the public.

January 3 — Massachusetts Memorial Hospitals, staff meeting. Page 999, issue of December 12.

January 4 — American Board of Obstetrics and Gynecology. Page 787, issue of November 7.

January 5–March 2 — Public Health Lectures. Cambridge Hospital. Page 1039, issue of December 19.

January 5–March 9 — Free Public Lectures. Harvard Medical School. Notice above.

January 7–31 — Joseph H. Pratt Diagnostic Hospital, medical conference program. Notice above.

January 9 — Pentucket Association of Physicians. Page 263, issue of August 15.

January 13, 14 — Third Annual Congress on Industrial Health. Page 999, issue of December 12.

January 14 — Harvard Medical Society. Page 41.

January 21 — South End Medical Club. Page 41.

February 20–22 — American Orthopsychiatric Association, Inc. Page 999, issue of December 12.

March 8 — American Board of Ophthalmology. Page 201, issue of August 1.

March 12–14 — New England Hospital Assembly. Hotel Statler, Boston.

April 21–25 — American College of Physicians. Page 1065, issue of June 20.

May 21, 22 — Massachusetts Medical Society, Boston.

June 2–6 — American Medical Association. Cleveland, Ohio.

District Medical Societies

ESSEX SOUTH

January 8 — Visceral Pain and Its Relief. Dr. James C. White. Danvers State Hospital, Hathorne.

February 5 — Gastric and Duodenal Ulcer: Diagnosis and treatment. Dr. Arthur Allen. Lynn Hospital.

March 5 — X-ray in Heart Disease. Dr. Merrill C. Sosman. Essex Sanatorium, Middleton.

April 2 — Pediatric Problems in General Practice. Dr. Joseph Garland. Addison Gilbert Hospital, Gloucester.

May 14 — Relation of the Doctor to the Law. Mr. Leland Powers. New Ocean House, Swampscott.

FRANKLIN

January 14.
March 11.
May 13.
Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

January 28 — Carney Hospital.
February 25 — Medicolegal meeting. 8:30 p.m. Hotel Puritan, Boston.
March 25 — To be announced.
May 8 — Censors' meeting. Hotel Puritan.

SUFFOLK

January 29 — Page 604, issue of October 10.
April 30 — Page 604, issue of October 10.

WORCESTER

January 8 — Worcester City Hospital, Worcester.
February 12 — Worcester State Hospital, Worcester.
March 12 — Memorial Hospital, Worcester.
April 9 — Hahnemann Hospital, Worcester.
Supper at 6:30 p.m. followed by a business meeting and scientific program.

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941

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Psychotherapy: Treatment that attempts to improve the condition of a human being by means of influences that are brought to bear upon his mind. By Lewellys F. Barker, M.D., professor of medicine, emeritus, Johns Hopkins University School of Medicine; visiting physician, Johns Hopkins Hospital, Baltimore. 12°, cloth, 218 pp. New York: D. Appleton-Century Company, Incorporated, 1940. $2.00.

A Surgeon Explains to the Layman. By M. Benmoscheé, M.D. 8°, cloth, 317 pp., with 62 illustrations. New York: Simon and Schuster, 1940. $3.00.

Psychiatric Social Work. By Lois Meredith French, director, Study of Trends, American Association of Psychiatric Social Workers, and psychiatric social worker and instructor in mental hygiene, New Jersey State Teachers College, Newark. 8°, cloth, 344 pp. New York: The Commonwealth Fund, 1940. $2.25.

The 1940 Year Book of Pathology and Immunology: Pathology. Edited by Howard T. Karsner, M.D., professor of pathology and director, Institute of Pathology, Western Reserve University, Cleveland. *Immunology.* Edited by Sanford B. Hooker, M.D., professor of immunology, Boston University School of Medicine, member, Evans Memorial for Clinical Research and Preventive Medicine, and immunologist, Massachusetts Memorial Hospitals. 12°, cloth, 688 pp., with 113 illustrations. Chicago: The Year Book Publishers, Inc., 1940. $3.00.

Compendium Physicae. By Charles Morton. Compiled about 1680. Vol. xxxiii of the publications of The Colonial Society of Massachusetts. 8°, cloth, 237 pp. Boston: The Colonial Society of Massachusetts, 1940. $5.00.

Man's Greatest Victory Over Tuberculosis. By J. Arthur Myers, Ph.D., M.D., professor of medicine and preventive medicine and public health, University of Minnesota, and chief of medical staff, Lymanhurst Health Center, Minneapolis. 4°, cloth, 419 pp., with 31 illustrations. Springfield, Illinois. Charles C Thomas, 1940. $5.00.

Multiple Human Births: Twins, triplets, quadruplets and quintuplets. By Horatio Hackett Newman, Ph.D., Sc.D., professor of zoology, University of Chicago. 8°, cloth, 214 pp., with 24 illustrations. New York, Doubleday, Doran and Company, Incorporated. $2.50.

The 1940 Year Book of Industrial and Orthopedic Surgery. Edited by Charles F. Painter, M.D., orthopedic surgeon, Massachusetts Women's Hospital and Beth Israel Hospital, Boston. 12°, cloth, 484 pp., with 299 illustrations. Chicago. The Year Book Publishers, Incorporated, 1940. $3.00.

The New International Clinics: Original contributions, clinics and evaluated reviews of current advances in the medical arts. Edited by George Morris Piersol, M.D., professor of medicine, University of Pennsylvania, Philadelphia. Volume IV, New Series 3, 1940. 8°, cloth, 326 pp., with 47 tables and 124 figures. Philadelphia: J. B. Lippincott Company, 1940. $3.00.

A Family Doctor's Notebook. By I. J. Wolf, M.D., professor of medicine, emeritus, University of Kansas School of Medicine. 8°, cloth, 315 pp. New York: Fortuny's, 1940. $2.00.

Blood Pressure Study: 1939. 4°, cloth, 69 pp. New York: compiled and published by The Actuarial Society of America and The Association of Life Insurance Medical Directors, 1940. $4.00.

BOOK REVIEWS

Operative Surgery. Volumes I and II, fifth edition. By J. Shelton Horsley, M.D., LL.D., and Isaac A. Bigger, M.D. With contributions by C. C. Coleman, M.D., Austin I. Dodson, M.D., John S. Horsley, Jr., M.D., and Donald M. Faulkner, M.D. 4°, cloth; Volume I, 768 pp., with 802 illustrations, and Volume II, 1567 pp., with 1391 illustrations. St. Louis: C. V. Mosby Company, 1940. $18.00 (set).

The title might lead one to think that this set of two volumes deals only with specific operations. Actually, the word "operative," has been used in its broadest sense, and includes physiology, diagnosis, indications for surgery and many other considerations so essential in obtaining good results.

All the surgical specialties are included, and some of the chapters have been written by authorities in the field. The scope of the work precludes a thorough discussion of some surgical problems, but a good balance is maintained in the editing of all but a few sections. Although the subject has some interest to the surgeon, the space devoted to ligation of arteries seems excessive in view of the relatively infrequent application of this procedure.

The chapters by Dr. Horsley, Sr., deserve special mention. The history, the references to recent contributions and the reasons for a procedure are presented with unusual clarity by this careful student of surgery. His results in complications of acute appendicitis are difficult to improve, and bespeak excellent practical judgment.

These two volumes serve as useful reference for the general surgeon and for the study of surgery in the medical curriculum.

Physical Therapy for Nurses. By Richard Kovács, M.D. Second edition, thoroughly revised. 8°, cloth, 335 pp., with 99 illustrations. Philadelphia: Lea & Febiger, 1940. $3.25.

This work is divided into seven parts: an introduction, "Heat," "Sunlight," "Electricity," "Water," "Massage," and "Exercise." These subjects are discussed from the standpoint of physics, physiological effects and technic of application. Although the author has had to be brief, and at times even dogmatic, his method of writing is fortunately such that he has managed to crowd into a small space a great deal of useful information. The tables, diagrams and photographic illustrations of apparatus and technic serve to clarify the text.

Although this book is intended for nurses and technicians who are expected ordinarily to carry out the treatments prescribed by the physician, it gives them, in addition to the technic of application, an insight into the motives or rationale for the employment of these therapeutic measures. It is a praiseworthy contribution to the furtherance of the education of nurses in physical therapy.

The New International Clinics. Original contributions: Clinics and evaluated reviews of current advances in the medical arts. Edited by George Morris Piersol, M.D. Vol. II, New Series 3, 1940. 8°, cloth, 365 pp., with 100 illustrations and 23 tables. Philadelphia: J. B. Lippincott Company, 1940. $3.00.

This volume is a valuable addition to the series. There are original contributions that deal with varied subjects, among them fungous infections, intermittent claudication associated with sclerotic lesions of the abdominal aorta, theoretical and practical considerations of vitamin K, pellagra therapy and fusospirochetosis.

In clinics by members of the faculty of Rush Medical College and the University of Chicago, the applied physiology of the testis, the glandular treatment of male hypogenitalism, malignant giant-cell tumors of the bones and many other interesting subjects are discussed.

The quality of *International Clinics* has long been demonstrated. This volume maintains the high standards of its predecessors.

An Introduction to Biochemistry. By William Robert Fearon, M.A., ScD., M.B., F.I.C. Second edition. 8°, cloth, 475 pp. St. Louis: C. V. Mosby Company, 1940. $3.75.

In the last few years, a great many texts have appeared on the subject of biochemistry. The author of each has often contributed to different aspects of the problem. Dr. Fearon adds more detail to the subject of chemistry itself and to the chemistry of each of the important component chemical units that take part in biological systems. However, the book is weak in the linking of each of the metabolic processes, and it is extraordinarily brief in discussing the functions of chemical entities. The reader should be warned of numerous mistakes throughout the text. For example, gram instead of milligram has been written in the text, and in the discussion of phosphoflavins, co-carboxylase is discussed instead of co-deaminase. The structural formulas for the sex hormones are erroneous and should be changed. The section on acid-base balance is incomprehensible, because of omission rather than commission. On the whole, the book cannot be recommended as an ideal text for the subject.

Green's Manual of Pathology. Revised and enlarged by H. W. C. Vines, M.A., M.D. Sixteenth edition. 8°, cloth, 1166 pp., with 701 illustrations. Baltimore: Williams & Wilkins Company, 1940. $8.50.

The sixteenth edition of *Green's Manual of Pathology* is divided into two parts, the first covering the general principles of pathology and the second concerned with the special pathology of organs in relation to clinical medicine. The chapters on bacteriology and parasitology have been omitted. Part I contains new chapters dealing with the process of repair of tissues and with the general character of tumors in the light of recent cancer research. In Part II the chapter on diseases of the blood and diseases of lymphatic tissue and the spleen has been replaced by a chapter on diseases of the reticuloendothelial system, in which the leukemias are included. There is also a chapter on the anemias.

Because pathology is not a static subject but reflects the continuous changes in the knowledge of diseases, factual material is often altered or augmented; an almost endless number of topics demand inclusion. As a textbook on pathology this volume is very difficult to evaluate because many very important subjects are necessarily omitted.

The arrangement of the various chapters conforms with the standard works in pathology already published in this country. There is an excellent chapter on immunity, allergy and infections, and the one on diseases of the ductless glands is especially informative. The book contains many illustrations, although many show relatively low magnification. Unfortunately, there are no references to the literature, which is a serious omission, since practically all American books on pathology have a voluminous bibliography that is especially useful to the laboratory worker. Except for this omission, the book can be recommended to medical students, because it covers thoroughly the basic facts in the study of pathology.

Psychology and Psychotherapy. By William Brown, D.M. (Oxon.), D.Sc. (Lond.), F.R.C.P. Fourth edition. 8°, cloth, 260 pp. Baltimore: Williams & Wilkins Company, 1940. $4.75.

The author states in the introductory chapter that he hopes this book "will provide the general reader not only with a grasp of the position and achievements of psychology and psychotherapy today—but also with a psychological basis for the study of politics and international relations." To fulfill this Herculean task, he begins with a presentation of some of the theories of Freud, Jung, Janet, Adler, Morton Prince and others, with the emphasis on Freud's concept of the unconscious and dreams. This portion of the book is followed by theories of the emotions and the author's experience in the treatment of psychoneurotic soldiers in World War I. The chief factors in his management of these cases consisted of persuasion, "whereby the patient was rationally convinced of the true nature of his symptoms," and hypnosis. Seventy per cent of the men returned to the line after an average of a fortnight's rest and treatment in the hospital. In view of such excellent results it is surprising to read later that the author let himself give "mental analysis to the utmost extent" and "suggestion treatment in the most vigorous form" to patients with Korsakow's syndrome due to alcohol. The poor results from psychotherapy in this group of cases were to be expected and might easily have fostered the author's mistaken notion that it is sufficient in a book on psychotherapy to enumerate the psychoses "and pass on, as they give little scope to psychotherapy."

The following are some of the titles of chapters in the latter half of the book: "Sublimation and Spirituality," "Suggestion," "Hypnotism and Faith" and the "Psychology of Peace and War." Here and there these chapters make interesting reading, but they contain little to recommend them to the physician seeking guidance with regard to clinical cases.

Atlas of Cardioroentgenology. By Hugo Roesler, M.D. F°, cloth, 124 pp., with 166 illustrations. Springfield, Illinois: Charles C Thomas, 1940. $8.50.

This book is more than a good collection of typical x-ray pictures. It is the work of a teacher with a gift for graphic presentation of his material. The x-ray appearances are well correlated with clinical, electrocardiographic and anatomical findings. The printer has achieved remarkably sharp reproductions of the x-ray films. The atlas will not take the place of a comprehensive text or reference book, but it does offer a most lucid introduction to the subject.